# Brain

## A Journal of Neurology

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DECEMBER, 1938

BRAIN.

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# TUMOURS OF THE THALAMUS—A CLINICO-PATHOLOGICAL STUDY.

BY G. E. SMYTH AND KARL STERN.

*(From the National Hospital, Queen Square.)*

THE following study was undertaken with two objects in view. The first was to determine whether the development of tumours in the thalamus is fortuitous and without special characteristics, or whether amongst the great variety of tumours involving this structure a group could be identified having some characteristic features, such as a peculiar mode of development or of expansion. Examination of the material available at the National Hospital appears to indicate that there is a type of glioma which, arising in the thalamus, tends to expand along the wall of the 3rd ventricle, the walls of parts of the lateral ventricle and of the iter, and to invade adjoining regions of the brain in a lateral direction rather than ventrally towards the tuber.

The second problem was concerned with the degree to which the symptomatology of thalamic lesions, as determined from the study of vascular lesions by Edinger (1891), Dejerine and Roussy (1906), Holmes and Head (1911), was reproduced by new growths.

We have been impressed by the discrepancy to be noted between the symptomatology of thalamic tumours and the classical thalamic syndrome. Therefore a study of the clinical picture of thalamic tumours seemed desirable. Six cases were studied for this purpose, and the record is amplified by the consideration of cases reported in the literature.

## MATERIAL AND METHOD.

The formalin fixed tissue was imbedded in celloidin and cut in serial sections. In view of the marked secondary mechanical and vascular

damage produced by tumours it appeared superfluous to undertake a detailed study of single nuclei and fibre tracts, and, therefore, it seemed adequate to stain each 25th section. Blocks had already been removed from each case for routine examination, and these gaps had to be reconstructed in the light of the macroscopical post-mortem photographs. The serial sections were stained by Nissl's method. In addition van Gieson's hæmatoxylin, Mallory's phosphotungstic acid hæmatoxylin, hæmatoxylin-eosin, Holzer's and Weigert-Pal's stains were applied to representative sections. Trial sections from various parts of the cortex were stained with Scharlach-R, Nissl's, and v. Braunmühl's stains in order to exclude general cerebral diseases.

TUMOURS INVADING THE THALAMUS FROM THE VENTRO-LATERAL PERIPHERY.

*Case 1.*—D. M., a man aged 50, was admitted to the National Hospital under Dr. Gordon Holmes on April 16, 1937.

The first symptom of his illness in August, 1936, was a persistent sensation of weakness of his right wrist. Within a few weeks there was a deterioration of fine movements of the fingers, and by December the right arm was weak and this was followed by slight weakness of the right leg. These disabilities slowly increased and two weeks before admission he became unable to shave himself. He did not admit to any sensation of numbness but suffered frequently from a dull aching pain in the right arm. For three weeks he had had severe vertical and occipital headaches which constantly awakened him at about 5 a.m. and lasted for the greater part of the day. Occasional brief diplopia on looking to the left had been present for one week and during this time there had been a persistent blurring of vision which, he insisted, was quite independent of diplopia. In other respects he felt well; appetite was good and, if anything, he was gaining weight. For about three weeks he had been sleeping unusually well and often had dozed during the day, a thing he had never done previously. The patient had been seen in private consultation by Dr. Gordon Holmes on March 24, 1937. At that time he complained of weakness and clumsiness of the right limbs and of numbness and aching of the right arm. Headache and visual disturbances had not then appeared. The significant findings recorded by Dr. Gordon Holmes were: Considerable weakness of the right lower face and deviation of the tongue to the right; marked loss of sensibility for prick, touch and temperature on the right half of the face with absence of the corneal reflex. There was no papillœdema, the visual fields were full and there was no abnormality of the extrinsic or intrinsic ocular muscles. The limbs on the right side were rather stiff and power was slightly reduced, proximal and distal segments being equally affected. There was considerable ataxia of the right limbs. The tendon-jerks were exaggerated on the right and the right plantar response was a doubtful extensor. On the right half of the body there was much sensory loss for touch, prick and temperature and great loss for posture, form and vibration. Dr. Gordon Holmes considered that the patient had a progressive lesion, probably neoplastic, deep in the left hemisphere and, from the amount of sensory disturbance, that it lay near the thalamus.

*Examination.*—April 16, 1937: The patient was a well-built florid man who co-operated well. Speech and intelligence were entirely normal. He was right handed.

Taste, smell, and hearing were normal. Vision was $\frac{6}{6}$ in each eye. On confrontation with a 5 mm. white disc there appeared to be a slight limitation of the right homonymous fields but this observation was not confirmed by subsequent perimetry. The fundi were normal. The external ocular movements were full. There was no nystagmus, ptosis or diplopia. The pupils were equal (5 mm. in diameter) and circular in outline. They were fixed to direct and consensual light but contracted promptly and fully on convergence. The jaw muscles were normal. There was a marked weakness of the right lower face in both voluntary and emotional movement. The tongue deviated to the right. There was hypoalgesia, hypoæsthesia and

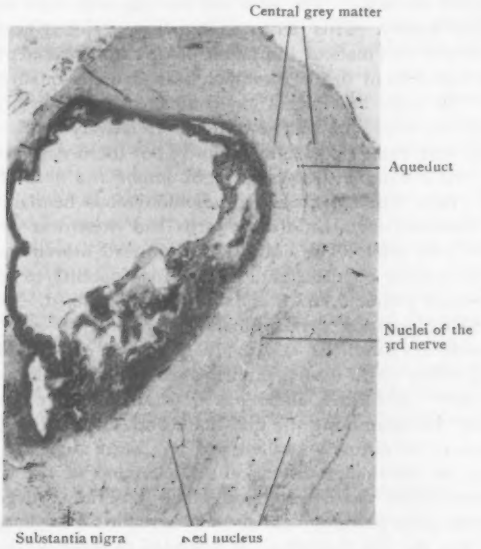


FIG. 1.—*Case 1.* Situation of the tumour in the rostral part of the mid-brain (Nissl. Approx. × 4.)

impaired temperature discrimination over the whole territory of the right trigeminus, and the right corneal reflex was less active than the left. The remaining cranial nerves were normal.

There was some hypertonus of the right arm and leg, and power was a trifle diminished. Tests for co-ordination revealed a gross ataxia of the right limbs. Alternating movements were carried out clumsily on the right.

On the right there were increased tendon-jerks, ankle clonus, diminished abdominal reflexes and an extensor plantar response.

There was marked impairment for touch, pain, pressure pain and temperature discrimination on the right half of the body. The area of sensory loss came to within one inch of the mid-line and was as deep on the trunk as on the periphery of the limbs. There was a gross loss of postural sensibility in the right arm and leg. The arm was the more severely affected and here the elbow and shoulder were

as much affected as the wrist and fingers. It was impossible to find a threshold for compass points on the right hand and there was a total failure of primary recognition when common articles were placed in the right hand. Vibration was not perceived on the right arm, on the right leg it was diminished.

The cardiovascular system was normal. Blood-pressure 150/100. Examination of other systems showed no abnormality.

*Cerebrospinal fluid.*—Initial pressure 140 mm. of water. Cells less than 1 per c.mm. Total protein 0·160 mgm. per 100 c.c. Globulin positive. W.R. negative in blood and fluid.

*Progress.*—April 26, 1937: Strong pin-prick caused an exaggerated response on the right half of the body. The pain was less tolerable than on the unaffected side and it radiated widely. This perverted response persisted until death.

May 6: There was marked limitation of upward movement of the eyes and an attention hemianopia in the right upper homonymous quadrants.

May 25: The right hemiplegia was complete and the arm and leg were flaccid. The tendon-jerks were diminished although relatively more active on the right. Both plantars were extensor. He sank slowly but there were great fluctuations from day to day. He alternated between a light stupor and deep coma.

June 3: There was a definite right homonymous hemianopia. The right eye was turned inwards and a little downwards and there was weakness of conjugate movement to both sides. The limitation of upward movement was not quite complete and was greater on the right. There was inability to converge. The pupils were rather small (about 3 mm.), equal and entirely fixed. Throughout the illness the pulse and temperature were normal.

*Post-mortem examination.*—The body of a rather thin middle aged man. Right arm and leg rather more wasted than the left (½ inch difference at the middle of the upper arm). The brain alone was examined. There was a slight cerebellar pressure cone. On examining the mid-brain both anteriorly and posteriorly the left crus was seen to be diffusely swollen and less white than the right. There was a slight degree of ventricular distension. On section of the fixed brain a circumscribed tumour mass was encountered which was rather degenerated and showed large greenish-grey gelatinous areas. It occupied the larger part of the left tegmentum and the left thalamus. It extended caudally to the level of the nucleus albus and orally up to the anterior part of the lateral nucleus of the thalamus. In its lower part it occupied the whole parabigeminal area and a lateral zone of the red nucleus leaving only a small rim of the superior colliculus intact. In its upper part it occupied the lateral part of the thalamus and the adjacent part of the internal capsule and the lenticular nucleus (mainly globus pallidus). The anterior and medial nuclei of the thalamus were macroscopically intact.

Microscopical examination showed a large-celled glioma with a marked tendency to degenèration. Apart from large glia cells (many of which were multinucleated or in mitosis) there were numerous smaller cells of various types. In some places there was a perivascular arrangement but this was not constant, many vessels showing no attachment to neuroglial cells. All varieties of degenerative change were seen in the nuclei of both large and small cells but mitoses were more common in the large cells. The vessels showed chiefly thickening of the media but intimal proliferation was seen in some. Although the tumour in its single elements was rather polymorphous, the appearances were essentially the same at all levels which were examined. From the great number of large multinucleated cells and from the

large protoplasmic astrocytes it resembled most closely the variation which Roussy and Oberling (1931) described as the giant cell astrocytoma.

Blocks from the material still available, were imbedded in celloidin and a series of 47 sections (20 $\mu$) was stained with thionin.

On attempting to reconstruct the tumour stereoscopically it was found to consist of an elongated cylindrical mass with irregular processes. It extended from the genu of the left internal capsule, at the level of the broadest extension of the lenticular nucleus, downwards to the level of the inferior colliculus. The greater part of the lenticular nucleus, the genu, and the anterodorsal part of the internal capsule were destroyed. The ventral part of the lateral nucleus, almost the whole of the zona reticulata, the ventral nucleus and the larger lateral part of the pulvinar had disappeared. The lenticular fasciculus and the zona incerta were entirely destroyed and here the tumour occupied the dorsal capsule of the subthalamic nucleus (Luys), compressing this nucleus and invading a small dorsolateral part of it. A process of tumour tissue extended through Wernicke's field into the most proximal part of the optic tract at the point nearest to the lateral geniculate body. The medial and lateral geniculate bodies lay within the zone of glial and mesodermal reaction surrounding the tumour. At this level the tumour occupied the greater part of the anterior colliculus and the area adjacent to it, the parabigeminal area (Mingazzini), the areas of the medial lemniscus, the dorsal portion of the quinto-thalamic tract, and the outer (more cellular) zone of the central grey matter and compressed the aqueduct into crescentic form (fig. 1). The red nucleus was much compressed, and its dorsolateral part was invaded by tumour tissue. At this point a lateral process of the tumour extended through the dorsolateral cell group of the substantia nigra into the corresponding segment of the peduncle. The most caudal part of the growth invaded chiefly the parabigeminal area, the more caudal level of the medial lemniscus and the lateral capsule of the red nucleus, interrupting many of the fibres of the oculomotor nerve as they passed forwards through the mid-brain.

SUMMARY.

Right hemiparesis with sensory disturbances conforming to the thalamic syndrome in a man aged 50. Later widespread ocular palsies occurred and death resulted after a total course of ten months.

Giant-cell glioma affecting the inferior part of the internal capsule and the lateral mesencephalic area. Expansion medially (thalamus, tegmentum) and laterally (lenticular nucleus). No immediate primary relation to the ventricular wall.

*Case 2.*—E. B. aged 43, a single woman, was admitted to the National Hospital under Dr. Gordon Holmes, on March 1, 1937.

For many years she had held a responsible post as a head saleswoman and until one week before admission her health had been good. Then quite suddenly, she began to complain of feeling excessively tired and she found herself continually yawning. This fatigue grew worse and she became unusually sleepy. Four days before admission to hospital she became aware that her left hand was weak. At the same time she thought that the right corner of her mouth had become drawn up During the course of the next two days the weakness of the left arm became so great that she was scarcely able to withdraw it from beneath the bedclothes and

movements of the fingers were quite impossible. On the morning of the day of her admission to hospital she found that the left leg had become rather weak and she was walking with a limp. To direct questions she said that she had been sleeping very heavily for about a week and she had no difficulty in sleeping for ten or eleven hours together. She denied ever having had any headache or pain elsewhere. There had been no disturbance of vision. The menses were regular and the last period had occurred about a fortnight before admission.

*Examination.*—March 1, 1937: The patient was a well-nourished, well-preserved woman. A degree of ptosis gave her a rather sleepy appearance, but she was alert and co-operated fairly well. Orientation was correct and there was no gross defect of memory. There was no apraxia in the unaffected (right) arm. She was right handed.

*Cranial nerves.*—Smell, taste and hearing normal. Vision $\frac{6}{6}$ in each eye. The visual fields were full to confrontation tests and there was no attention defect or visual disorientation. The fundi were normal.

The external ocular movements were full and there was no nystagmus or diplopia. The pupils were unequal (right 4 mm., left 3 mm.) and slightly irregular in outline.

They were fixed to direct and consensual light but reacted moderately well on convergence. There was a moderate bilateral ptosis, rather more marked on the left, with overaction of the frontalis.

There was a doubtful hypoalgesia on the nose which seemed rather more definite on the left. Sensibility to light touch was normal. Both corneal reflexes were present but the left was less brisk than the right. Marked weakness of the left lower face was well brought out in ordinary conversation. It was very little marked when she smiled or laughed. When the mouth was maintained widely open the left arch was not so well preserved as the right.

The remaining cranial nerves were normal.

*Motor functions.*—Upper limbs: There was no wasting, fibrillation or involuntary movement. The left arm lay helplessly by her side and was quite toneless. Enough power remained at the shoulder to maintain the arm outstretched for perhaps a second. There was trace of voluntary flexion and extension at the elbow, but the paralysis was complete below the elbow. Firm grasping with the right hand caused feeble associated flexion of the left arm. The functions of the right arm were entirely normal. The lower limbs showed neither wasting nor fibrillation. There was a very slight hypertonus of the left leg. Power was slightly reduced in all muscle groups of the left leg. There was no inco-ordination. The functions of the right leg were normal. The sphincters were unaffected.

Reflexes: Both ankle-jerks were absent, the other tendon-jerks were normal. On the left the superficial abdominal reflexes were absent and the plantar response was extensor.

Sensation was everywhere normal for prick, touch, temperature discrimination and vibration. Appreciation of posture and direction of movement was normal in the fingers and toes. Discrimination of compass points was normal in the hands and feet.

Cardiovascular system: Heart enlarged to the left, the apex beat being six inches from the mid-line; a long systolic murmur at the apex was conducted upwards over the aortic area. No diastolic murmur was heard. Pulse 70. Blood-pressure 90/65 mm. Hg. The other systems were normal.

*Progress.*—March 2, 1937: Slight sensory loss was observed in the left hand.

Discrimination of compass points was faulty and there was slowness in identifying common articles placed in the left hand.

March 15: The pupils were more irregular than on admission and totally inactive to light. The left leg was slightly hypertonic. For the first time it was possible to demonstrate a slight hypoalgesia on the left limbs and trunk. There was marked loss of postural and 2-point discrimination in the left hand and foot, the hand being the more affected.

March 30: She complained of headache and vomited once. There was blurring of the nasal halves of the optic discs and marked inability to look upwards. On confrontation there was slight limitation of the left homonymous fields. From this time she slowly became demented, but there were brief intervals in which she was able to recognize her friends. She suffered from considerable headache. The fundi remained unchanged and, although the discs were blurred, no measurable swelling appeared.

In general the signs remained unchanged; the hemiplegia gradually became spastic until the rigidity of the left arm and leg were intense and the superficial sensory loss became more marked. However, the loss of sensibility to prick never became complete, and to the end she vigorously resented strong stimuli. At no time did she complain of anything resembling spontaneous pains. The "thalamic response" was never detected, but it must be remarked that for many weeks before her death a proper sensory examination was impossible. The condition of the pupils and external ocular movements during the time she was under observation were of particular interest.

April 12: Both pupils were totally inactive to light, the left pupil reacted only slightly on convergence; the right was fixed. Paralysis of upward conjugate movement was first noted on March 30 and it was then complete. However, twelve days later there was some slight ability to elevate the eyes. Conjugate paralysis was again complete after a further two weeks, and remained so until she died. The power of convergence was lost about the beginning of May, and from that time until her death in June her eyes appeared to be entirely immobile. The size and shape of the pupils varied considerably from time to time. At times they were equal in size, more often the right was slightly the larger. In the last two weeks of her life they became moderately dilated, and the right was permanently rather the larger. The degree of irregularity also showed great variability from day to day. Perimetry was carried out shortly after admission and the fields were full. Later a left homonymous defect was detected, and confirmed on numerous occasions but her condition did not allow then of perimetry. The cerebrospinal fluid was examined on March 2. It was under an initial pressure of 120 mm. of water. It contained 0·180 per cent. of total protein but otherwise showed no abnormality. The Wassermann reaction was negative in blood and fluid.

*Post-mortem examination.*—The body of a very wasted, middle-aged woman. No external signs of disease. *Brain*: Arteries healthy. There was no swelling of the pons or mid-brain, but on examining the thalamus on the two sides after incision of the corpus callosum that on the right was definitely the more bulky. On incision a rounded mass of tumour was seen in the right thalamus. There was no significant lesion in the spinal cord or viscera.

On section of the brain in the horizontal plane the cortex in the calcarine region on both sides was found to be shrunken, brownish and softened. There was no evidence of thrombosis or other disease of either posterior cerebral artery. There

was a greyish soft area in the mid-brain in the region lateral to the red nucleus and central grey matter. The tumour was a soft rounded or oval fairly defined brownish mass extending through the thalamus from near its upper surface down to the tegmental region of the mid-brain on the right side. It was not available for study in its entirety as portions had previously been removed for routine pathological examination. From what remained it could be seen that the tumour occupied the whole of the lateral part of the thalamus and appeared to invade to some extent the internal capsule. The medial part of the thalamus appeared less invaded. The anterior nucleus appeared quite free from growth. It was impossible to delimit the tumour more exactly for the reason already stated.

*Microscopical examination.*—The tumour was composed of small rounded cells with rather irregularly sized nuclei. There were very numerous and thin-walled vessels in the tumour and numerous threads of reticulum and collagen in the matrix. Vessels of medium size were cuffed with tumour cells. The cells showed many mitoses, chiefly irregular, and there was a great tendency to degeneration. The appearances were those of meningeal sarcomatosis. There was no resemblance to a glioma.

In the calcarine cortex the nerve cells had disappeared, leaving an area of glio-mesodermal reaction in the deeper layers and a swelling and proliferation of macroglia in the surface layers.

From the remaining part blocks were imbedded in celloidin and serial sections (every 25th section) were stained with thionin. In the basal ganglia the tumour occupied the larger part of the lenticular nucleus and the ventro-lateral zone of the thalamus, replacing the whole sector of the intervening internal capsule. Only a small (dorsal) part of the globus pallidus and the dorsal and lateral zones of the putamen were preserved. The tumour had obviously destroyed parts of the ansa lenticularis. The substantia innominata (Reichert), the nuclei of the tuber and the paraventricular nucleus were preserved. The medial areas of the thalamus were not invaded. In the dorsal part of the medial nucleus there was a small area of an apparently fresh softening. In the central third of the pes pedunculi there was an area of tumour which extended through the zona reticulata and pars dorsalis of the substantia nigra into the field of the medial lemniscus. In its neighbourhood, in the substantia reticularis, near the central grey matter, there was a small area of recent softening. It could not be determined whether or not the mesencephalic area of tumour was in connection with the main part of the tumour. In the central grey matter, around the aqueduct, there was a diffuse proliferation of capillaries and glia.

## Summary.

*Clinically*: Left hemiparesis and, later, severe sensory loss in a woman aged 43. Reflex iridoplegia occurred early in the disease which proved fatal after a course of three months. Signs of increased intracranial pressure and dementia occurred late in the disease.

*Anatomically*: Round cell sarcoma of the internal capsule expanding in both directions; into the thalamus from the periphery towards the ventricle, and into the lenticular nucleus. Area of growth in the ventrolateral area of the mid-brain. Bilateral infarction of the visual cortex.

### Comment.

These two cases have this in common that distinct focal symptoms, such as are met with in other cases of capsular or thalamic lesions, were the initial symptoms and dominated the clinical picture almost to the end. The first patient suffered from contralateral hemianæsthesia and hemiparesis; the second developed first a hemiplegia and, soon afterwards a hemianæsthesia; in both the pupils were fixed to light. Leaving aside for the present this last-mentioned symptom and those which developed at a late stage, we may accept the predominant and initial symptoms (hemiparesis, hemianæsthesia) as typical of a capsulothalamic lesion. Neither of these cases can be regarded as a primary thalamic tumour. They occupied part of the internal capsule, the fillet system, the lateral and ventral mesencephalic areas and extended in two directions: medially towards the 3rd ventricle and laterally towards the lenticular nucleus. In other words, whatever the site of origin of the tumour, whether in the lateral or ventral mesencephalic areas or in the internal capsule contiguous to the thalamus, it is clear that the thalamus was first invaded in its lateral and ventral regions.

The first case was a typical giant-cell glioma (Roussy and Oberling) and it is noteworthy that the duration of life was longer than in the other cases. The second case was more interesting from a histological point of view. With its round cells, which either spread as a compact growth or permeated the Virchow-Robin spaces, it resembled closely the cases of primary round-cell neoplasms of the brain (Fried 1926, Környey 1934, Scheinker 1936, Mage and Scherer 1937). It is remarkable that the four similar cases reported by previous authors also occupied the basal ganglia, probably arising from the meninges of the base. As in this case hemiplegia was the first symptom it is conceivable that the tumour originated in the pes pedunculi and expanded in upward direction. If this is so it might explain the early loss of pupillary reactions.

### Intrinsic Thalamic Gliomas.

*Case 3.*—T. C., a man aged 64, was admitted to the National Hospital (Dr. Gordon Holmes) on September 9, 1932. The details of the history were confirmed and supplemented by his wife.

In April, 1932 he was suddenly discharged from his employment because of business depression and this caused him great anxiety. Up till that time his health had been good although he had always been of a "nervy" disposition. From this time he became unusually tense and was obviously brooding over his trouble but no certain mental or physical defect was noted until some six weeks before admission to hospital when he noticed a gradually increasing weakness of the right side of the body affecting the upper limb rather more severely than the lower. At about the

same time he began to complain of "coming queer" in his head and that the right arm and leg felt cold. His wife first realized that he was seriously ill when she discovered that his handwriting had degenerated into a scrawl and that he was unable to handle a pen. About August 20 he began to suffer from severe headaches. These he attributed to constipation. They were accompanied by nausea but he never vomited. He was himself aware of a deterioration of memory and was aware of, although not distressed by, his inability to recollect the details and chronology of his illness. He had always been a restless sleeper taking a long time to get off to sleep. Latterly this had not been so and in addition he was often drowsy by day. No disturbance of speech had been noted. No fits had occurred. He was right handed.

FIG. 2.—*Case 3.* The lateral nucleus is invaded by tumour growth which here stops short accurately at the border towards the internal capsule. It is noticeable even at this magnification that the nerve cells in this area are preserved. (Nissl. × 14.)

*Examination.*—September 9, 1932: The patient was a tall rather thin and ill looking man who suffered from frequent and severe headache. He was inclined to be drowsy but, when roused, was quite alert. Mentally he showed a striking loss of memory together with some inattention. As noted above he gave a disjointed and incomplete history. He answered incorrectly or not at all such questions as "What hospital are you in?" "When and where were you born?" "When were you married?" He did not retain an address or any digit of a series of 7. Judgment and insight were certainly impaired, for, despite professions of concern for the future of his family, he made flippant replies when asked what would he do when cured. His attention could not be held for more than a few seconds. He smiled vacantly from time to time. There was no aphasia or apraxia.

His handwriting was only just legible but the paresis and sensory loss in the right hand were sufficient to account for this.

Vision was $\frac{6}{6}$ in each eye. The fields were full on confrontation and perimetry. The optic discs were thought to be a little blurred and the retinal veins somewhat overfull, but these observations were not confirmed by Mr. Williamson-Noble when he examined the fundi a week later. The pupils were equal (4 mm.), slightly irregular and reacted briskly to direct and consensual light and in convergence. The external ocular movements were full in all directions. There was no nystagmus, squint or diplopia. There was a very questionable bilateral ptosis. The jaw deviated slightly to the right when opened against resistance. There was definite weakness of the right lower face which was accentuated by sustained voluntary movement. Sensibility on the face was normal. The corneal reflexes were present and equal although somewhat sluggish. The remaining cranial nerves were normal.

There was a mild right hemiparesis. The loss of power was somewhat greater in the leg than in the arm. The posture of the right arm was very poorly sustained. Tone was normal in the arm, but was slightly increased in the right leg. There was a very gross inco-ordination in the right arm and leg which was independent of vision.

On the right the tendon-jerks were exaggerated, and there was ankle-clonus ; the superficial abdominal reflexes were absent and the plantar response was extensor. On the left the reflexes were normal except for an equivocal plantar response.

Sensation was difficult to assess. He was incapable of co-operating for more than a few seconds. Perception of light touch and vibration appeared to be normal. Pin-prick was perhaps a little dulled over the right hand, elsewhere it was normally felt. Sense of position and passive movement appeared to be altogether absent in the right extremities but were normal on the left. Compass tests were attempted but the patient persisted in repeating the same answer.

Examination of the other systems did not reveal any abnormality. Pulse and temperature remained within normal limits throughout. The urine was normal in constitution and amount. The *cerebrospinal fluid* was examined on September 9, 1937. It was under a pressure of 100 mm. water. There were three small and medium sized mononuclear cells per centimetre. The total protein was 0·130 mg. per cent. and the globulin test was weakly positive. In other respects the fluid was normal. The W.R. was negative in blood and fluid.

Stereoscopic radiograms of the skull did not show any abnormality.

*Progress.*—September 22, 1937 : He was distinctly more alert and free from headache (daily enemata of 50 per cent. magnesium sulphate had been given since September 15). With the eyes closed he had no notion of the position of the right arm and leg. Slight hypoalgesia and hypoaesthesia was confirmed on the right side, particularly in the upper extremity.

September 29 : There was a marked increase in the mental symptoms and a severe nominal aphasia. Power was still very good on the right side although a little diminished by comparison with the left. The inco-ordination on the right side was even more marked than on admission. It resembled cerebellar ataxia. The right plantar response was strongly extensor, the left was doubtful.

After this the patient's condition steadily deteriorated and death occurred from a terminal pneumonia.

*Post-mortem examination.*—The body of a very thin elderly man. No external sign of disease. Brain only removed. The dura was tense and the convolutions flattened. On opening into the ventricles, which were considerably dilated, a large softened tumour bulged into the left ventricle in the region of the basal ganglia.

It pushed the bend of the ventricle backwards behind that on the right side. Post-mortem examination of the internal organs showed bronchopneumonia, healed nodular tuberculosis of the apices, atheroma of the aorta and a double renal pelvis on one side.

On section of the fixed brain in the coronal plane a tumour was seen in the left basal ganglia occupying an area which extended from the level of the pineal body posteriorly to the level of the infundibulum anteriorly. In its anterior and lower parts it was white and firm causing a diffuse swelling of the thalamus. The upper and posterior parts were hæmorrhagic and diffusely brownish red. Here the tumour pushed the middle part of the lateral ventricle and, further back, pressed across the mid-line. It appeared to involve almost the whole of the left optic thalamus. In the middle part, where the tumour was soft and hæmorrhagic, a very small rim of the thalamus along the medial (ventricular) surface seemed to be preserved. In its anterior part the internal capsule seemed to be infiltrated to a small extent.

*Microscopical examination.*—The tumour was composed of large cells with one or two peripherally placed nuclei and numerous fine processes. It was very degenerated in its upper part but very few multinucleated cells were seen in it and no mitoses were visible. It appeared to be a large celled astrocytoma. In serial sections (53 sections, 20$\mu$, Nissl) the tumour was first seen at the anterior tip of the thalamus compressing, but not invading, the adjoining part of the caudate nucleus. There was an area of tumour infiltration around the vena terminalis. In large parts of the lateral nucleus and the medial nucleus in the anterior planes the tumour occupied the whole of the thalamus but the nerve cells were still seen in these areas (fig. 2). More caudally the tumour again consisted of vast degenerated areas in which nothing of the destroyed tissue was visible. It expanded laterally into the internal capsule in its posterior third and in its sublenticular part. Dorsally and medially it extended into the pulvinar which was entirely replaced by tumour tissue. Here it expanded laterally into Wernicke's field and infiltrated the medial fifth of the lateral geniculate body in its dorsal part. Ventrally it did not expand into the region of the vegetative hypothalmic nuclei neither did it reach the mid-brain caudally. In the mesencephalic level a considerable zone of the ventral nucleus and of the medial nucleus (nucleus reuniens, Malone) was preserved. The tumour nowhere came into the area of the eye muscle nuclei or of the red nucleus. On the lateral and ventral surfaces of the pulvinar the tumour expanded into the wall of the inferior horn, compressing and partially infiltrating the ventricular surface of the hippocampus and the white matter surrounding the inferior horn. It stopped short at the U-fibres of the cortex of the temporal lobe. The basal ganglia on the right side were normal apart from a zone of subependymal gliosis which separated the right thalamus from the ventricle. Trial sections from the frontal lobes and cerebellum, stained with Nissl and Scharlach R, were normal.

## Summary.

*Clinically*: A man aged 64 showed a rapidly developing right hemiparesis with pronounced sensory loss. Mental deterioration occurred early and became deep before death which occurred some six months after the onset of symptoms.

*Anatomically*: There was a large celled astrocytoma, with a marked

tendency to degeneration, which occupied the left thalamus with the exception of a small area in the posterior planes of the medial and ventral nuclei. The mid-brain and the eye muscle nuclei were intact. The internal capsule in its posterior third and sublenticular portion were partially infiltrated. There was also an infiltration of the white matter surrounding the inferior horn and of the hippocampus on its ventricular surface.

*Case 4.*—W. G., a man, aged 67, was admitted to the National Hospital under Dr. Gordon Holmes on April 4, 1937.

The history was obtained from a son who said that his father had always had good health until the onset of his present illness. In the middle of February, 1937, some six weeks before admission to hospital, he caught influenza. He took to his bed and seemed very weak. He was a little "light headed," but no attention was paid to this as it had often been noted before if he chanced to be feverish. However, when the fever remitted in the course of a few days these mental symptoms did not clear up. He continued to be unusually weak and his mental condition was abnormal. In describing the mental state as "light headed," the son meant a childish and rather fatuous manner. His speech was perfectly intact but his remarks were constantly silly and irrelevant and the family could place no reliance on his statements. He continued in much the same state until a week before admission to hospital and then speech began to fail rapidly. This was first apparent by a failure to select the proper word but, within a few days, he was quite unintelligible and incapable of reading or writing. From the beginning of his illness he had been unusually sleepy but in the last few days this had become more marked. Headache first appeared at the time when the drowsiness increased but there was no vomiting. On the day of admission there were several outbursts of great excitement and violence. He seized anything at hand to throw at his wife and terrified the whole family. Vision was unaffected, at any rate up to the onset of aphasia. He had been incontinent of urine and fæces for one day.

*Examination.*—April 4, 1937: A well-nourished man in no evident pain and quite alert. He was right handed. The presence of an almost total aphasia made thorough examination difficult. His speech was unintelligible, being nothing more than a string of unconnected words. He was unable to read or write and he did not appreciate pantomime. He showed imperfect recognition of common articles. When handed a pencil he had no notion of how it should be held. There was some degree of apraxia. When given a box of matches he at length recognized its nature but it was only after fumbling for several minutes that he succeeded in extracting and striking a match. He showed no distress at or insight into his condition but smiled constantly.

*Cranial nerves.*—Smell apparently normal. Visual acuity not determined. He frequently shut his left eye, particularly if he wished to look at anything; and he had a marked disinclination to look towards the right. On confrontation there was a considerable right homonymous hemianopia, but perimetry could not be used. The fundi were normal. The external ocular movements were full, although there was disinclination to look to the right. There was no obvious squint, ptosis, en- or exophthalmos. The pupils were equal (3 mm.), very slightly irregular in outline and almost fixed to direct and consensual light. Convergence could not be obtained. There was a pronounced weakness of the right lower face which was very noticeable

in ordinary emotional play. The tongue came out straight. There appeared to be some diminution of sensibility to prick over the right half of the face but the corneal reflexes were present and equal.

The remaining cranial nerves were normal.

The right arm and leg were moved less than the left. When support was withdrawn from the outstretched arms the right fell away at once. Voluntary movements were slightly weaker on the right. There was a peculiar irregular and rather coarse tremor of the right arm. It was only present when the limb was unsupported and, if anything, was more palpable than visible. More exact tests of co-ordination could not be applied. The tendon-jerks were slightly increased on the right and there was clonus of the right foot. All the abdominals were absent. Both plantars were flexor but the right toes tended to fan. To crude tests with pin-prick there was a definite hypoalgesia on the right trunk and limbs. Examination of other systems did not disclose any abnormality, except for a moderate arteriosclerosis. The blood-pressure was 170/120 mm. Hg. The urine was normal.

Cerebrospinal fluid: Pressure, 300 mm. water. Fluid yellow. Cells 25 per c.mm. (2 per cent. polymorphs, 10 per cent. large mononuclears). Total protein 0·40 per cent. Globulin test strongly positive. W.R. negative in blood and fluid.

*Progress.*—There was progressive deterioration. To exclude the possibility of a subdural hæmatoma trephine holes were made and the ventricles were tapped. The exploring needle encountered a solid tumour deep in the left hemisphere. He died one month after admission to hospital.

*Post-mortem examination.*—The body of an old man, rather thin, no external signs of disease. The brain only was removed. The dura was moderately tense but there was no evidence of cerebellar pressure cone. No softening of convolutions was visible externally but the left temporo-parietal region felt bulkier than the right, and on opening into the lateral ventricles, a brownish tumour mass was seen filling the left optic thalamus and projecting into the third ventricle. Its central part was gelatinous on section, and actual tumour substance appeared as a very thin layer. The tumour extended backwards from the optic thalamus to the occipital white matter external to the ventricle. Anteriorly it passed upwards to the superior surface of the thalamus, and laterally to the lenticular nucleus, leaving only a part of the ventral nucleus of the thalamus macroscopically intact. The exact extension in the hypothalamic region could not be defined in the material still available. In its lateral parts the tumour invaded large areas of the white matter. In the occipital lobe the growth stopped short beneath the U fibres of the cortex.

*Microscopical examination.*—In its undegenerated parts the tumour was composed of astrocytes of very varied size and shape, but with very well defined fibres forming a moss-like background. Many of the larger cells had large cell bodies but rarely more than one or two nuclei. Mitoses were only seen in the endothelial cells of the vessel walls. On approaching the degenerated areas the cell nuclei became pyknotic and many of them showed karyorrhexis. In these areas mitotic figures were seen. The tumour was an astrocytoma but with more tendency to polymorphism and degeneration than is shown by most tumours of this type.

In serial sections (45 sections, 20 $\mu$, Nissl) the tumour extended from the anterior tip of the thalamus, including the anterior nucleus, to the posterior tip of the pulvinar. In its anterior levels it pushed a small preserved rim of grey matter into the ventricle and upwards towards the corpus callosum. In dorsal direction it stopped short at the vena terminalis, compressing to a certain extent the caudate nucleus but

not invading it. In ventral direction it did not occupy the whole thalamus. The ventral nucleus was preserved in large part. Even parts of the lateral nucleus were preserved, or in some levels its nerve cells were preserved though invaded. Thus the tumour had not invaded the hypothalamic region or the mid-brain. Its chief extension was in a lateral and posterior direction. It occupied the posterior and inferior part of the internal capsule, the posterior part of the lenticular nucleus, and almost the entire white matter of the temporal lobe lateral to the inferior horn. Nowhere did it reach the cortex itself. Wernicke's field was partly invaded. For the most part the tumour was confined to the pulvinar and stopped accurately at its lateral and inferior borders. The lateral geniculate body itself was free. The tapetum, Gratiolet's radiation and the inferior longitudinal bundle were replaced by tumour tissue. The subependymal glia surrounding the vena terminalis was proliferated at levels where there was no actual tumour. Apart from this there was an even subependymal gliosis on the ventricular surface of the caudate nucleus.

SUMMARY.

*Clinically*: A man, aged 67, showed a rapidly developing mental deterioration which was followed by slight right hemiparesis with some sensory loss. Reflex iridoplegia was present early in the disease.

*Anatomically* this tumour was an astrocytoma, replacing almost the whole left thalamus, except for parts of the ventral nucleus. It had a tendency to grow along the ventricular wall and to expand in a posterio-lateral direction. Thus, apart from the thalamus, it had destroyed chiefly the secondary optic system, the internal capsule and part of the lenticular nucleus.

*Case 5.*—R. B., a man aged 63, was admitted to the National Hospital under Dr. Riddoch on February 8, 1937. By birth a Bulgarian he had lived in England since childhood and, until the onset of his present illness, had enjoyed excellent health. The following history was obtained from his wife:—

About one month before admission he first complained that his near vision had become poor. He went to a spectacle maker who gave him lenses but these did no good. Indeed he was rather worse off for he complained that, when reading, the print appeared double and to overcome this he acquired the habit of closing his left eye. At this time his family became aware of a slight change in his disposition. Previously he had been mentally and physically active but now he was slow and this slowness day by day became more evident. He was noticed to take an unusually long time in dressing and his replies to quite simple questions were delayed. First he lost the ability to write and his attempts at writing became a mere childish scribble. At this time he became unable to read. He was often seen with a newspaper in his hands but he never turned the pages and merely stared vacantly at whatever was before him. Soon after this his speech began to fail. His articulation was correct but he put his words together badly. At times however he spoke remarkably well. His memory had become grossly unreliable in the past two weeks. He never alluded to the distant past but recent happenings were hopelessly mixed up. His temper had become uncertain. For about two weeks he had been excessively sleepy. His gait was noticed to be slightly unsteady about a week before admission.

He did not veer to one side more than another. His general health seemed unaffected. His appetite was very good ; indeed better than usual. There was no loss of flesh. He had never complained of headache and when directly questioned, denied ever having had any. There had been no vomiting. For perhaps two weeks he had often been seen to play with his fingers, touching one after another with the thumb, now with one hand, now with the other. His wife thought that this was an imitation of one of the tests which his doctor had used.

*Examination.*—February 19: The patient was a spare elderly man, unable to give a history by reason of a severe dementia. To direct questioning he said that his eyes were wrong but in what way could not be ascertained and no admission of diplopia was obtained. He constantly screwed up his left eye. He explained

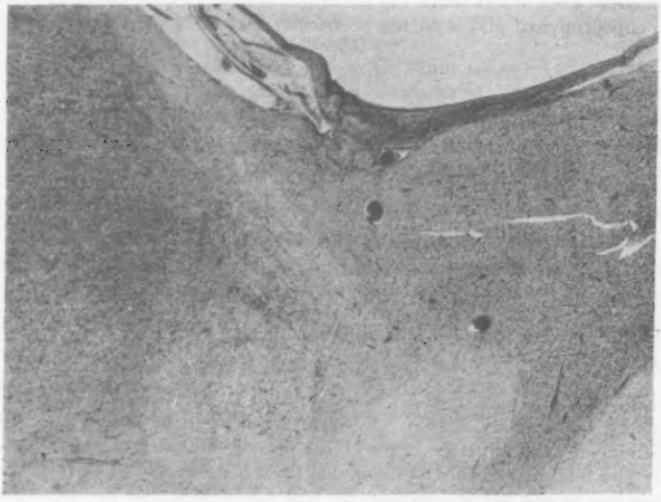

FIG. 3.—*Case 5.* The anterior border of the tumour coincides with the anterior border of the thalamus. The ganglion cells in these areas (lateral nucleus) are preserved. Note the subependymal gliosis over the ventricular surface of the caudate nucleus. (Nissl. × 12.)

that he first did this to overcome double vision but he would not say why he still did it. He was disorientated in time and space and he was quite unable to carry out the simplest mental arithmetic. There was no apraxia but he was slow and clumsy in using his hands. On one occasion he attempted to put some coins in what he imagined to be an inside pocket of his pyjama jacket. He was able to dress himself, but had to be reminded to get into each garment separately.

He never spoke unless spoken to. His replies were correctly phrased and articulated but he was slow and halting and used as few words as possible. It was impossible to obtain a specimen of his handwriting. When given a pencil he held it for several seconds and then threw it down saying he could not see to write. He made the same excuse in explanation of his partial inability to read. When urged he

read slowly and words of more than two syllables gave him great difficulty. When shown a series of common articles he misnamed several. He used the word pencil to describe a pocket torch, a fountain-pen and a penknife when these were shown to him in succession. Despite the dementia, co-operation was remarkably good provided commands were given in a simple direct form. He was right-handed.

He appeared to recognize but could not name any of the usual test odours (peppermint, cloves and camphor). The sense of smell was less acute in the left nostril. Vision approximated $\frac{6}{24}$ in each eye. The visual fields were full by confrontation

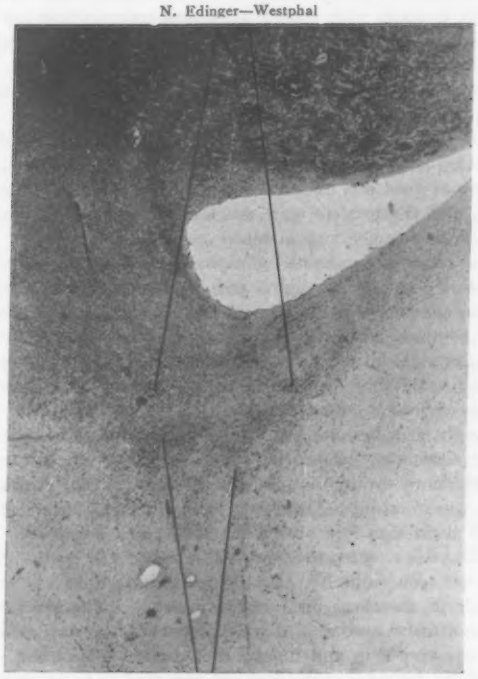


FIG. 4.—*Case 5.* Relation of the posterior margin of the growth to the eye muscle nuclei. (Nissl. Approx. × 13.)

tests and there was no attention defect or visual disorientation. Perimetric charts were not obtainable because of the dementia. The fundi were normal. Hearing was slightly reduced in both ears; Weber was not lateralized and air conduction was better than bone conduction on both sides. There was complete paralysis of upward movement of both eyes, both voluntarily and reflexly. The other external ocular movements were full and there was no nystagmus or diplopia. The pupils were small (2 mm. in diameter), equal and regular in outline. There was only the merest trace of contraction to direct and consensual light. There was complete

inability to converge. There was no ptosis, en- or exophthalmos. The other cranial nerves were normal. Sensation on the face was intact, and the corneal reflexes were equally brisk.

There was no wasting, fibrillation or involuntary movement. Tone was natural in all the limbs and active movements were normally strong. There was no tremor or inco-ordination, and alternating movements were carried out equally well on both sides. His gait was slightly unsteady but no more to one side than the other. The tendon-jerks were present and equal upon the two sides. The superficial abdominal reflexes were all present and both plantar responses were flexor.

Pin-prick, light contacts with cotton wool, and temperature discrimination were normally and equally perceived on both sides of the body. Appreciation of passive movement and direction of movement was normal in all four limbs. Discrimination of two points was normal on the hands and feet. Firm pressure on the calves evoked a normal and equal response.

There was no sign of any cardiovascular disease. The vessels were healthy. Blood-pressure 115/70 mm. Hg. The other systems were normal.

The *cerebrospinal fluid* was under a pressure of 140 mm. of water. It contained 1 cell per c.mm., and the total protein was 0·09 per cent. In other respects it was normal, and the W.R. was negative in blood and fluid.

*Progress.*—His condition remained stationary except that, after a few days, the pupils became totally inactive to light, and on February 24 ventriculography was performed. It was considered likely that he had a neoplasm in or about the posterior part of the third ventricle and this assumption was supported by the ventriculogram which showed incomplete filling of the posterior end of the ventricle. The shortness of the history suggested that the neoplasm was invasive and therefore inoperable. He gradually passed into a comatose state and died on March 9. In the last few days of life the right arm became flaccid and motionless and he developed bilateral extensor plantar responses. Repeated examinations of the fundi confirmed the absence of papillœdema throughout the entire course of the disease.

*Post-mortem examination.*—The body of a wasted rather elderly man. No external signs of disease except burr holes for ventriculography. The brain only was removed. The dura mater was very adherent to the skull.

Brain tissue was seen to be herniated into the burr holes. There was, however, no other evidence of increased intracranial pressure. The posterior aspect of the mid-brain was seen to be swollen and white, especially on the left side, and the left optic thalamus was very firm and bulged into the third ventricle.

On section of the fixed brain the tumour appeared to be limited to the left optic thalamus and to involve practically the whole of this structure. It did not appear to involve the mid-brain except in a small area in the region of the left superior corpus quadrigeminum. It extended toward the medial wall of the posterior horn where it bulged the intact ventricular wall into the ventricle. Laterally it apparently invaded the internal capsule for a small distance but a large part of the lateral and ventral nucleus of the thalamus seemed intact. It extended through the massa intermedia into the medial area of the right thalamus. At its frontal end it seemed to stop short at the caudate nucleus.

*Histological examination.*—The tumour was rather polymorphous. In the most rostral levels (about the level of the anterior thalamic nucleus) there were a large number of oval cells in an indefinite matrix. They were uniformly dense and in some planes followed the direction of the myelin fibres. There were no mitoses.

The whole appearance at this level was rather like that of a diffuse pontine glioma. The character of the neoplasm changed considerably at the levels posterior to this. Here the density varied from place to place. There were areas of necrosis and pseudorosettes. At these levels indeed the tumour might have been classified as a glioblastoma. Even here, however, mitoses were very rare.

Blocks of the basal ganglia extending from the middle of the lenticular nucleus down to the caudal part of the red nucleus were imbedded in celloidin and serial sections were cut (every twenty-fifth section, Nissl).

*Left side*: The medial thalamic nuclei were entirely destroyed. In the posterior areas they were replaced by tumour tissue.

In the anterior levels (level of the anterior nucleus) the medial nucleus (dorso-medial nucleus) was invaded by tumour cells but the ganglion cells were preserved. The posterior and inferior parts of the medial nucleus together with the centre-median nucleus and nucleus arcuatus and nucleus semilunaris had disappeared. The lateral nucleus was preserved in the dorsal levels. In the lower parts and caudal two-thirds the lateral and ventral nuclei were either partially infiltrated by tumour or completely destroyed.

The anterior nucleus was preserved except for a slight gliosis at its postero-inferior edge. The mamillo-thalamic tract (Vicq d'Azyr) seemed intact. The pulvinar was completely destroyed.

In the posterior part of the third ventricle the tumour formed a bridge to the ventricular wall of the opposite side. The anterior part of the superior colliculus was invaded. The tumour extended with a long process along the medial wall of the inferior horn, and was attached to the cortex of the hippocampal area. A part of the cortex of the area glomerulosa (Economo) was destroyed by compression. The internal capsule was slightly invaded in its posterior part adjoining the thalamus. The zona reticulata was free to a large extent. In some parts the edge of the tumour coincided exactly with the border of the thalamus (fig. 3). The ventricular nucleus was free from tumour. Some cells of the globus pallidus were swollen with eccentric nuclei. The nucleus of Edinger showed a marked gliosis on the left side and a slight one on the right. The somatic nucleus of the 3rd nerve was intact. The left nucleus commissuræ posterioris (Darkschewitsch) was infiltrated by tumour cells (fig. 4). The substantia innominata of Reichert was intact. The mamillary bodies, the nuclei of the tuber, and the supraoptic nuclei were intact. A dorsal (accessory) part of the paraventricular nucleus was slightly infiltrated. The corpus subthalamicum and the lateral geniculate body were intact.

*Right side*.—The tumour had invaded the massa intermedia and medial areas of the adjoining thalamus. The ganglion cells in these invaded areas appeared intact. The subependymal glia separating the medial thalamic nucleus from the ventricular wall had proliferated to a marked extent.

Trial sections from various parts of the cortex did not reveal any abnormality.

## Summary.

*Clinically*: A progressive dementia in a man aged 63 ending in death within two months of the first symptoms. Reflex iridoplegia was an early sign. Motor and sensory signs were absent till within a few days of death.

*Anatomically*: Diffuse glioma of the left thalamus spreading along the ventricular wall across the massa intermedia to the opposite side, and

extending to the most anterior part of the aqueduct and along the inferior horn. Its mode of expansion was such that the latero-ventral thalamic areas were obviously the last to be affected.

*Case 6.*—E. E., a woman aged 44, was admitted to the National Hospital under Dr. C. P. Symonds on September 10, 1937.

The family history was uneventful. The only noteworthy detail in her past medical history was a questionable history of slight Graves' disease in 1921. She had always been of an intensely active disposition, "heading for a breakdown for several years." Her pulse was habitually rapid.

On June 14, 1937 (i.e. some three months before admission) she had what seemed an ordinary attack of influenza and was in bed for three days with malaise, catarrh, aching in the limbs and some fever. When she got up her pulse was rapid and she

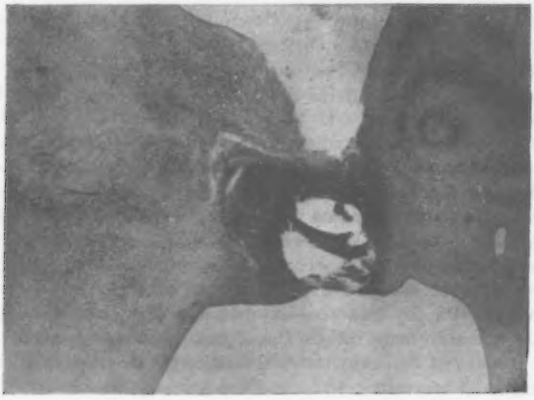

FIG. 5.—*Case 6.* The massa intermedia is occupied almost symmetrically by tumour tissue. (Nissl. × 10.)

was put on Bellergal. Three days later she complained that everything seemed out of focus and when reading she was shutting one or other eye to stop the lines running together. The pupils were noticed to be dilated. She found tennis impossible as she was always missing the ball. At this time she became unusually drowsy and she could sleep at any time of the day, and this symptom had been present to some extent ever since. Early in July she had one severe bursting headache and ever since she had complained of a constant buzzing over the head.

A tentative diagnosis of encephalitis lethargica was made. Towards the end of July there was a severe attack of giddiness. Since then she had often felt dizzy and unsteady. In July and August headaches became more frequent, and she felt a pressure at the back of her neck. Six days before admission she began to vomit, and this lasted for three days. The headache was now less severe. She stated that her hearing had grown much worse but her husband thought it still very good. Her memory had been poor for some weeks, she could not concentrate and was hazy about dates. No change in temperament was admitted. Her speech was

unaffected. No fits or faints had occurred. Libido had been failing for two years and absent for the past year. The menses were scanty and rather irregular.

*Examination.*—A thin woman weighing only 7 st. She was unable to give a history and could neither date the onset of her symptoms nor give their evolution. Her memory, especially for recent events, was very bad and she had forgotten events of the past week. She was very confused. She retained six and sometimes seven digits. She could not subtract seven from hundred. Marked inattention and disorientation were present. She was rather drowsy but co-operated fairly well when stimulated. Her mood was normal but she had very little insight. Her speech was normal.

*Cranial nerves.*—Smell normal. V.A.R. $\frac{6}{6}$. V.A.L. $\frac{6}{6}$. Fields full on confronta-

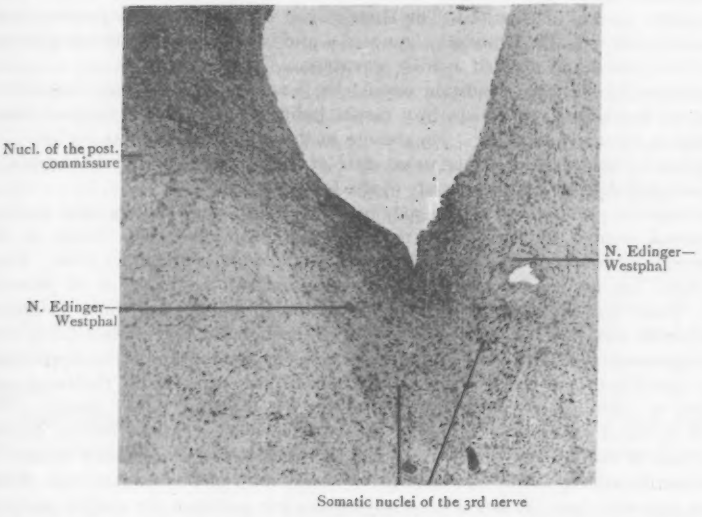


FIG. 6.—*Case 6.* Relation of the posterior margin of the growth to the eye muscle nuclei. (Nissl. × 18.)

tion with a 3 mm. white object. Fundi normal. The pupils were equal and of moderate size, slightly irregular in outline and displaced a little inwards; absolutely inactive to light but still reacting, though feebly, on convergence. Convergence was almost absent. Slight convergent squint was present at rest with constant nystagmoid jerking, the quick component being inwards. The eyes were directed a little downwards and there was complete paralysis of conjugate upward movement, which persisted when the head was bent forwards. Conjugate downward movement was slightly limited. There was marked weakness of both lateral recti, the right more than the left; and slight weakness in conjugate movement to the right; the left eye did not quite reach the inner canthus. There was no nystagmus on movement, no ptosis or proptosis. She did not complain of diplopia at the time

of examination. There was no deafness. The remaining cranial nerves were normal.

Apart from some general asthenia there was no abnormality of the motor system. The tendon-jerks were all brisk. The superficial abdominals were feeble. Both plantar responses were indefinite but there was much voluntary movement. Sensation was entirely normal.

*General examination.*—Temperature rather low, 97·4° F. Pulse about 70-80, blood-pressure 115/90. *Urine* normal except for a trace of albumin. S. G. 1022. *Cerebrospinal fluid* (September 13, 1937) initial pressure 110—140 mm. water. The fluid was clear and colourless and no cells were seen. The total protein was 0·120 per cent. and the globulin tests were weakly positive. The W.R. was negative in blood and fluid.

*Progress.*—September 16: There were marked apathy, indifference, lack of insight and a general inattention. The latter was so marked that she appeared deaf, but was not really so. Dr. Symonds diagnosed a mid-brain tumour in the neighbourhood of the pineal and decided against operation.

September 30: General condition worse; she was very drowsy; and complained of frequent headaches but always in a casual indifferent way. She vomited often, especially in the early morning. No change in the physical signs was found.

October 5: She seemed in her usual state at 8 p.m. but was found in coma at 10.30 p.m. and died in the early hours of the following morning.

*Post-mortem examination.*—The body of a rather thin small middle-aged woman. No external sign of disease. Only the head was examined. The bones of the vault were very thin but there was little evidence of erosion of the inner table. Dura fairly tight but no great flattening of convolutions and no evidence of pressure cones. There was slight bulging of the infundibular region, and some distension of the lateral and third ventricles. On cutting through the splenium a fairly well defined tumour, reddish-brown in colour, was seen growing from the upper part of the quadrigeminal plate. It was attached to the right optic thalamus and appeared to infiltrate the posterior part of the left thalamus fairly deeply. The tumour occupied almost the whole of the anterior quadrigeminal bodies, leaving only a part of the left one and a small rim of the posterior commissure intact. It pressed on the right pulvinar and seemed to occupy the right habenular area. From there it expanded into the left side occupying the left pulvinar, the medial posterior parts of the left thalamus, and the centre-median nucleus at about to the level of the massa intermedia. The ventral nucleus seemed to be compressed but not infiltrated, the lateral nucleus and anterior part appeared intact. The internal capsule, the pes pedunculi, the red nucleus and the substantia nigra were also macroscopically intact.

*Histological examination.*—The tumour was very cellular and consisted of bipolar cells with oval rather elongated darkly staining nuclei and very ill-defined cell bodies. Many multinucleated cells of larger size were present, and some of these had ring nuclei or degenerated masses of chromatin, but no definite mitoses were seen. There was very little evidence of degeneration in the tumour.

In serial sections (20 $\mu$, Nissl, every 25th section stained) the tumour began caudally at the caudal end of the quadrigeminal plate which was occupied almost completely. Within the quadrigeminal plate the tumour was practically symmetrical and extended ventrally no further than the most dorso-lateral tip of the oculomotor nuclei. Further forward it became asymmetrical.

On the left it expanded from the anterior colliculus forward and outward into the pulvinar which was for the most part replaced by tumour tissue. The whole of the medial nuclei of the thalamus, and the nucleus arcuatus, nucleus semilunaris, and centre-médian nucleus were replaced by tumour tissue.

The ventral nucleus was partially infiltrated. The lateral nucleus was only invaded to a slight degree; its main part was intact. The anterior nucleus was intact. In its rostral parts the tumour became gradually smaller and was confined to the areas of the medial nucleus which immediately adjoin the ventricular wall.

Orally it ended within the massa intermedia where it had an almost symmetrical position extending a little to both sides (fig. 5). In its caudal parts it extended latero-ventrally into the mesencephalic part of the medial lemniscus.

More orally it broke through the border of the ventral nucleus into Forel's field H and the zona incerta. It also broke through the lateral border of the pulvinar into Wernicke's field. The lateral geniculate body was free. The tumour touched the fronto-lateral tip of the red nucleus, and infiltrated the nucleus of the posterior commissure (Darkschewitsch) (fig. 6).

On the right the tumour extended from the anterior end of the superior colliculus into the medial areas (nucleus reuniens of Malone). Along the wall of the 3rd ventricle a small process passed forward but did not reach the massa intermedia to rejoin the tumour from the other side. Because the thalami had been torn apart it could not be certainly decided whether or not there was a bridge across the ventricle between the tumour on the left and that on the right.

## Summary.

A woman, aged 44, who showed progressive dementia and ocular disturbances over a period of four months. Motor and sensory signs were absent.

*Anatomically*: Diffuse glioma with symmetrical anterior and posterior limits (massa intermedia and quadrigeminal plate). In between these two limits it expanded chiefly to the left. The localization of this tumour was very similar to that of Case 5 except that here there was no extension along the inferior horn of the lateral ventricle.

## Comment.

Clinically these cases were characterized by the fact that symptoms of mental impairment such as inattention, disorientation, confusion, emotional disturbances (Case 4) and sleep disturbances (Case 5), together with iridoplegia, dominated the clinical picture, and that, on the other hand, marked sensory and motor focal signs (hemianæsthesia, hemiplegia) were late in onset or poorly developed (Cases 3 and 4) or completely absent (Cases 5 and 6).

Case 3 is not easily distinguishable from the two cases in Group I except

that mental impairment and drowsiness dominated the picture from the very beginning. This case stands in between the cases in the first group and the last two cases in which focal symptoms, except the eye symptoms, were almost completely absent ; the picture in fact was that of a progressive mental deterioration combined with fixed pupils.

Anatomically these gliomas have produced a final picture of grossly irregular invasion and destruction. Nevertheless they have some important features in common which justify their consideration as forming a single group. All of them were related to the ventricular wall ; none of them extending in rostral direction further than the vena terminalis. In the opposite direction they extended into the tegmentum of the mid-brain, involving the iter and the adjacent nuclei (Cases 5 and 6), and along the wall of the inferior horn (Cases 3, 4 and 5). This relation to the ventricular wall and the adjoining areas might be explained as secondary invasion by a tumour of the depth of the hemisphere. However, a comparison of the areas of complete tumour growth, either degenerated or undegenerated, with the areas in which the preserved nervous structures were evenly infiltrated by tumour cells, makes it clear that all these tumours had originated medially somewhere near the ventricular system and that they had expanded from there laterally into the hemisphere. Thus the internal capsule in its posterior third and sublenticular part, the white matter surrounding the inferior horn (Cases 3, 4 and 5), the subthalamic zone in Forel's field H near the body of Luys, and Wernicke's field lateral to the pulvinar were invaded. As far as the thalamus was concerned it was striking that the lateral and ventral nuclei were invaded but showed intact nerve cells or were in part completely free. This was most striking in Cases 5 and 6, and it is noteworthy that these were the cases in which sensory symptoms were entirely absent. There was an obvious tendency for the growths to stop short at the borders of grey or white matter so that the edge of the tumour coincided with the border of the thalamus (figs. 3 and 4). This, however, was only observed where the infiltration was recent and the invaded structure was not yet destroyed. At a more advanced stage the tumour masses expanded irregularly but the border towards the caudate nucleus at the vena terminalis was, even then, fairly well preserved (fig. 3). There was a subependymal gliosis in other parts of the ventricle where there was no actual gliomatous tissue. In none of these cases were the so-called " vegetative " nuclei of the hypothalamus invaded. Only in Case 5 a small dorsal accessory part of the paraventricular nucleus lay within the marginal zone of the growth.

## Cases in the Literature.

Few cases in the earlier literature are described fully. Usually they are mentioned as "Glioma of the thalamus" or "tumour of the third ventricle" or "glioma of the basal ganglia," and the anatomical diagnosis is briefly stated. Nevertheless an attempt was made to find similar clinical and anatomical features in order to discover, if possible, the typical features of such cases.

Mott (1898) remarked that tumours of the 3rd ventricle may be mistakenly diagnosed as "general paresis." Henneberg (1905) stated that tumours of the 3rd ventricle do not produce any focal symptoms but marked mental disturbances of a variable character. Pfeifer (1910), in his paper on psychic disturbances occurring in tumours of the brain, described three cases of glioma of the basal ganglia. Two of them were confined to the thalamus, in one the corpus striatum was invaded and there was adjacent softening. In all three cases there was a combination of severe mental impairment and disturbance of the pupillary reflexes so that the picture was similar to that of general paresis. Pfeifer, from a study of 86 cases of cerebral tumour, came to the conclusion that the mental symptoms occurring in tumours of the basal ganglia were no local sign, and only dominated the picture because of a lack of focal symptoms. Lewison and Alter (1923) described a case of glioma of the thalamus which did not show any focal symptoms. It was complicated by hæmorrhagic retinitis and optic neuritis which had led to amaurosis. The tumour protruded into the ventricle. Högner (1923) found disturbances of the pupillary reactions in 4 out of 20 thalamic tumours. He did not, however, mention the exact site of the growths. Seletzki (1927) described a tumour of the thalamus with no focal symptoms whatever. Alfred Meyer (1928) described a glioma of the thalamus which corresponded conspicuously with our "intrinsic" group. Both thalami were affected in their medial parts. The tumour expanded subependymally and in lateral direction. Meyer emphasized that at some levels it stopped short precisely at the lateral border of the thalamus. At posterior levels the field of Forel and the body of Luys were infiltrated. The tuber was free. The tumour extended backwards to the pineal gland. The main clinical symptoms were: fixed pupils, in the first stage pyramidal symptoms, later the tendon-jerks were diminished, there was drowsiness and a lack of attention and interest. The patient's intelligence, however, was not impaired. Because of radiological evidence of aortitis a diagnosis of lues cerebri was made.

Ody (1932) examined in Cushing's clinic 25 cases of tumours affecting the basal ganglia, and reached the conclusion that there were no focal

symptoms characteristic of the basal ganglia. He emphasized particularly the complete absence of extrapyramidal motor signs such as athetosis, chorea, rigidity and tremor, a point which is confirmed in the present cases. The photograph of a thalamic glioma which he showed corresponded exactly in its mode of expansion with our " intrinsic " type of tumours.

Foerster and Gagel (1934) in describing a cyst of the 3rd ventricle discussed the relation between the diencephalon and mid-brain and emotional tone. According to them an antagonism exists between the two regions, for stimulation of the anterior part of the floor of the 3rd ventricle causes excitement and euphoria whilst destruction leads to apathy and somnolence. Reverse effects are produced by stimulation of the posterior part of the floor of the 3rd ventricle and the quadrigeminal plate.

More recently Riddoch (1936) described two cases of dementia which were caused by tumour of the 3rd ventricle. There was neither papilloedema nor increase of cerebrospinal fluid pressure, but hydrocephalus was severe and to this the dementia was attributed. In the case recorded by Mage and Scherer (1937) of a round-cell sarcoma which had a particular tendency to expansion round the 3rd ventricle, marked mental symptoms without local signs dominated the picture for a long time. The authors emphasize the same regarding the cases in previous literature (Fried, Környey, Scheinker).

In 1937 Baasch studied in Marburg's institute a glioma of the thalamus, aqueduct and pineal region. The patient had presented a picture of apathy with marked signs of internal hydrocephalus but no gross motor or sensory disturbance. The growth occupied the dorsal and medial parts of both thalami and was in its mode of expansion very similar to Meyer's case and to the present cases in Group II. The hypothalamus was unaffected. The tumour had a characteristic relation to the ependyma, and in its development it showed a very varying appearance at different levels. Baasch could distinguish five different types of growth each of which corresponded to a distinct type of Bailey and Cushing's classification. The largest part showed an appearance similar to that of diffuse gliomas of the pons (c.f. our Case 5). Because of its mode of expansion Baasch assumed that this glioma was of multicentric origin in the subependymal matrix. Hasenjäger (1938) examined in Spatz' laboratory 10 cases of glioma spreading along the ventricular walls. In one cross section of the brain she demonstrated two tumour masses, one in the thalamus and one in the lateral ventricle which, however, were parts of the same tumour. Besides this large mass she observed small neoplastic granulations in parts of the ventricle, and therefore she, too, came to the conclusion that these gliomas have a widespread " multicentric " origin.

## Discussion of Results.

It is fully recognized that the essentially topographical nature of this investigation is by no means free from objection. Nevertheless the congruities between the cases themselves, and their many points of agreement with similar cases drawn from the literature, indicate the likelihood that a critical survey of symptoms in relation to the site of the tumour will give information of value.

In the accompanying table the 6 cases are grouped according as to whether the medial or lateral regions of the thalamus were primarily affected by tumour and it is at once apparent that this pathological division coincides with certain striking differences in the clinical picture.

In Group I (Cases 1 and 2) the tumours had destroyed a large part of the lateral and ventral regions of the thalamus and, clinically, gross sensory disturbances were present from an early stage of the disease. These were of the type commonly encountered in thalamic lesions ; the threshold for all sensory stimuli was raised but the impairment of postural and discriminatory sensibility was disproportionately great. The complete thalamic syndrome was present in only one case (Case 1) and here the initial symptoms were unpleasant sensations of cold about the right elbow and hand. Despite a marked hypalgesia on the right trunk and limbs pin-prick was peculiarly intolerable and this perverted response was widely diffused. The rarity with which the thalamic syndrome results from a neoplastic lesion is widely recognized. Possibly the time factor is of importance and it is perhaps significant that in Case 1 the duration of the disease was relatively long. In this group the significant pathological finding was the more or less complete destruction of the ventrolateral part of the thalamus and close histological examination made it plain that this region had been invaded early in the disease. In this respect these two cases offered a striking contrast to the four in Group II for here the more medial parts of the thalamus were most severely affected and it was evident that the tumour had spread into the lateral thalamic region at a comparatively late stage of the disease (fig. 7). Thus in Group II, whereas the ganglion cells in the region of the medial nuclei had entirely disappeared, the ganglion cells in the lateral and ventral nuclei were still well preserved and, indeed, in places the structure of these nuclei was entirely normal.

Clinically in none of these four cases were sensory disturbances among the initial symptoms and in two (Cases 5 and 6) they were completely absent, at any rate until the onset of the terminal coma. The absence or insignificance of objective sensory disturbances in those cases in which the ventrolateral thalamic areas were intact, or at least invaded very late in

## TABLE OF CASES.

### GROUP I.—VENTROLATERAL THALAMIC TYPE.

| Case | Primary site of tumour | Initial symptoms | Motor signs | Sensory signs | Ocular signs | Mental deterioration | Evidence of hydrocephalus |
|---|---|---|---|---|---|---|---|
| 1.—D. M. aged 50 | Peduncular, capsulothalamic glioma | Paræsthesia | Hemiparesis (early), ataxia | Present at an early stage (thalamic syndrome) | Reflexiridoplegia at a late stage | Absent | Slight ventricular dilatation |
| 2.—E. B. aged 43 | Peduncular, capsulothalamic sarcoma | Monoplegia | Hemiplegia (early) | Early and severe sensory loss | Reflexiridoplegia at a late stage | Late in onset | Slight ventricular dilatation |

### GROUP II.—INTRATHALAMIC TYPE.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 3.—T. C. aged 64 | Intrathalamic glioma | Mental deterioration (?) | Slight hemiparesis, gross ataxia | Difficult to assess but sensory loss certainly present | Ptosis (?) | Early and progressive | Considerable ventricular dilatation |
| 4.—W. G. aged 67 | Intrathalamic glioma | Mental deterioration | Slight hemiparesis and marked tremor | Definite sensory loss | Reflexiridoplegia probably early | Early and progressive | Ventricles of normal size, but c.s.f. pressure of 300 mm. water |
| 5.—R. B. aged 63 | Intrathalamic glioma | Mental deterioration | Absent until the terminal phase | Absent | Reflexiridoplegia and paralysis of upward gaze, probably very early | Early and progressive | Ventricles of normal size (c.s.f. pressure 140 mm. water) |
| 6.—E. E. aged 43 | Intrathalamic glioma | Mental deterioration. Internal ophthalmoplegia (?) | Absent throughout | Absent throughout | Reflexiridoplegia and paralysis of upward gaze | Early and progressive | Slight ventricular dilatation, c.s.f. pressure, 110 mm. water |

the disease, stands in striking contrast to the gross sensory symptoms met with in those cases in which the tumour was primarily capsulo-thalamic.

This contrast receives added interest from its bearing on the probable anatomical equivalent of the thalamic syndrome. Since the original

description of this syndrome by Déjerine and Roussy (1906) it has been not uncommon to encounter relatively large thalamic lesions which, during life, gave no indication of their presence. The absence of sensory loss in such cases has always been puzzling for, until very recently, it was generally believed that the fillet system ended in relation with the whole of the thalamus and, therefore, it seemed inexplicable that destruction of any

considerable part of the thalamus should be compatible with a state of normal sensibility. As a matter of fact the resolution of this difficulty was given by Dejerine and Roussy (1906) and by Holmes and Head (1911) for in all their cases the lesions were confined to the ventral and posterior thalamic regions. Recent anatomical studies on the connection of the primate thalamus by Le Gros Clark (1932, 1935, 1938) and Earl Walker (1937) and the confirmatory experimental investigations of Dusser de Barenne and Sager (1937) have proved conclusively that the fillet system (medial lemniscus, spinothalamic tract, quinto-thalamic tract) terminates exclusively in the ventral thalamic nucleus and that the medial nucleus is not directly concerned with the mediation of impulses underlying sensation. If these observations are true for man they afford a satisfactory explanation for the integrity of sensation in those cases in which the ventrolateral part of the thalamus is either intact or invaded so late in the disease that the state of sensory functions cannot be ascertained.

The presence of a greater or less degree of hemiparesis in the cases in which the tumour had invaded the internal capsule and its absence in the two cases (Cases 5 and 6) in which the tumour had affected predominantly the medial part of the thalamus are entirely consonant with the view put forward by Dejerine and Roussy that hemiparesis is no part of the thalamic syndrome and, when present, is indicative of, and strictly proportionate to the extent to which the internal capsule is affected. It is interesting to note that a marked inco-ordination was present in three of the cases and, on the other hand, that there was no trace of inco-ordination in the two cases (5 and 6) in which the tumour was predominantly medial in position. The inco-ordination took the form of an action tremor and was entirely independent of visual control. In all three cases it appeared to be greater than could be accounted for by the weakness and sensory loss, and in Case 3 it was so gross that cerebellar disease was suspected. Ataxia has always been regarded as highly characteristic of the thalamic syndrome and it has often been reported in cases in which no other motor disturbances were present. The observations of Le Gros Clark and Earl Walker show that a large number of crossed fibres from the superior cerebellar peduncle passes to the region of the ventrolateral thalamic nuclei and from thence a further relay of fibres passes to the motor cortex. From this it would appear that the motor cortex receives impulses from the opposite dentate nucleus through the intermediary of the thalamus and interruption of this cerebello-frontal pathway is a possible explanation for the inco-ordination which may result from thalamic disease.

Disorders of ocular movement were present in five of the six cases here

reported and, except in Case 1, they made their appearance at any early stage of the disease. Reflex iridoplegia was the commonest abnormality. being present in all five, but in three of the cases an associated paralysis of upward gaze was present at the time of admission to hospital. The frequency with which similar palsies have been reported in cases of thalamic tumour has already been mentioned and it is interesting to consider the possible mechanisms of their production. Actual invasion of the oculomotor nuclei was minimal except in Case 1 and it appears highly improbable that the very early onset of these ocular palsies was related to direct invasion of the nuclei, particularly as initially the palsies were strictly in terms of conjugate movement. A much more probable explanation is that there was interference with the supranuclear pathway. As Collier (1927) has pointed out there is good reason for believing that the paths for the light reflex and for upward and downward conjugate movement undergo a partial decussation in the posterior commissure, and, more recently, Magoun *et al.* (1936), by electrical stimulation in monkeys of the region of the posterior commissure and periaqueductial grey matter, have added experimental support to clinical observation. The tumours in the present series of cases showed a marked tendency to extend caudally towards the level of the posterior commissure and it is to this that the early ocular palsies are attributed. These ocular disturbances are of considerable practical importance for unless their possible significance is borne in mind, relatively benign conditions such as neurosyphilis or encephalitis may be diagnosed and the more grave lesion overlooked.

With the exception of Case 1 mental deterioration was prominent in the six cases studied and it becomes of some interest to inquire into the probable factors which determined its development. Attempts to relate mental functions to specific regions of the brain have seldom proved satisfactory and tumours in particular are generally unsuitable for such purposes. The concomitant hydrocephalus which is usually present and vascular disturbances and dislocation of cerebral tissue must often introduce factors the effects of which cannot be estimated. It is generally accepted that increasing apathy, confusion and finally coma are the common results of progressive hydrocephalus but, in regard to the mental defects consequent on destruction of brain tissue *per se*, Symonds (1931) has expressed an opinion, widely held, that mental deterioration is related to the total amount of white matter destroyed rather than to destruction of any particular region of the brain. For these reasons critical consideration of the mental state in Cases 1, 2, 3 and 4 is valueless. The tumours were large and had led to abnormally high intracranial pressure and ventricular dilatation.

Cases 5 and 6 were, however, much more interesting. In these two patients the tumours were relatively well circumscribed and there are indeed very good reasons for assuming that the lateral part of the thalamus was invaded at a late stage of the disease. The absence of detectable sensory disturbances in these two cases has already been discussed but the reason for the early and severe mental deterioration is by no means at once obvious. In neither case was the type of mental deterioration particularly unusual or suggestive. It was characterized by progressively increasing inattention, forgetfulness and disorientation. One of the patients (Case 5) rapidly developed a global dementia at a time when drowsiness was completely absent ; the other (Case 6) did not become quite so grossly demented and here too there was no great evidence of abnormal drowsiness until within a few hours of death. In neither were signs of increased intracranial pressure at all marked, indeed apart from complaints of occasional headache in Case 3 they were entirely absent, and, finally, post-mortem examination disclosed a quite minor degree of ventricular dilatation. The frequency with which grave mental deterioration accompanies tumours in the region of the 3rd ventricle has already been alluded to but, whatever the cause of the dementia in many of these cases, neither ventricular dilatation nor massive destruction of white matter offers a reasonable explanation for its occurrence in Cases 5 and 6. It is therefore permissible to seek some more direct relationship between lesions of the medial part of the thalamus and the presence of a severe degree of dementia.

The observation of Le Gros Clark (1932), Le Gros Clark and Boggon (1935), and Earl Walker (1937, 1938) are pertinent in this connection for they have brought forward convincing evidence that the medial thalamic nucleus (n. dorso-medialis) projects exclusively to the granular frontal cortex and, furthermore, that this same nucleus is closely connected with the hypothalamus through the intermediary of the periventricular nuclei. It must be pointed out that in Cases 5 and 6 the tumour had extended across the massa intermedia into the opposite medial thalamic nucleus and it may be that this bilateral invasion of the medial thalamic nuclei was an important factor in determining the occurrence of dementia. This explanation is admittedly conjectural but it is at least worthy of consideration.

Having indicated the relationship that existed between the topography of these tumours and their symptomatology it seems necessary to outline the pathology of the intrinsic thalamic gliomas.

The isolation of well-defined types of tumour, based not so much on mere cytology but on their site of predilection and mode of expansion, has proved fruitful in the pathology of neoplasms in general and, more par-

ticularly, in relation to the pathology of meningiomas. The gliomas of macroglial origin appear to occur with almost equal frequency in all parts of the brain and to expand irregularly and this is probably one of the principal reasons why all classifications have been based solely on the morphology of the individual tumour cells. The cytology of the four gliomas in Group II may be dismissed with brief reference. All were astrocytomas in the broad sense of the term : the tumour cells showed a varying degree of differentiation and malignancy both in different parts of the same tumour and in the several tumours themselves. In all four cases the tumours were intimately related to the lateral wall of the 3rd ventricle but in this region the cells were either differentiated astrocytes having a rich fibre network, as in adult subependymal astrocytes, or more primitive elongated cells with fewer processes or fibres. In neither case did they bear any resemblance to the primitive spongioblasts attached to the ependyma or to the cells of the primitive subependymal matrix. The appearance of the subependymal zones in these cases differed only in degree of development from the very small gliomas of the aqueduct which Shelden *et al.* (1930) have described. This similarity is remarkable because it indicates that the subependymal glia may actually be the point of origin of these gliomas. This conjecture is reinforced when it is remembered that the mode of expansion of the tumours such as occurred in Group II and in similar cases reported in the literature (A. Meyer, Baasch, Hasenjäger) showed, not only the peculiar attachment to the ventricular wall (which would cause no surprise in gliomas of the thalamus), but also expansion in the direction of the aqueduct, along the inferior horn of the lateral ventricle, and anterior to the vena terminalis towards the caudate nucleus. The most recent infiltrations were always found either in the lateral zones of the thalamus or in the white matter of the hemisphere. A most interesting common factor in all four cases was the complete integrity of the tuber. This does not, of course, imply that the hypothalamus as such is resistant to gliomatous growth. The invasion of this region is not uncommon in gliomas of other localizations (fornix, optic nerve) and, therefore, the integrity of the tuber in these cases of intrinsic thalamic glioma must be related to the nature of the growths themselves. Opalski (1934) in his study on the normal histology of the ventricular walls made an interesting observation in this connection when he pointed out that the subependymal glial layer is normally absent in the region of the tuber and the paraventricular nuclei. Elsewhere in the 3rd ventricle the subependymal glial layer is comparatively thin but it is noteworthy that in the region of the thalamus the

fibrillary astrocytes normally extend into the area of the medial thalamic nuclei (Opalski). These observations all favour the hypothesis that the subependymal glial layer gives rise to the intrinsic gliomas of the thalamus. The term "intrinsic" in this respect, however, does not mean that these tumours originate exclusively in the thalamus. There was no sign that the areas of tumour in the roof of the mid-brain or neighbourhood of the lateral ventricle were of more recent origin. Hasenjäger's observations of small subependymal nodules of tumour growth in various places independent from one another and the diffuse subependymal gliomatosis in our Cases 5 and 6 favour the view that these tumours are of diffuse or "multicentric" subependymal origin. There is no resemblance between the cellular morphology of these tumours and the subependymal gliomas described by Roussy and Oberling (1931) as occurring in tuberous sclerosis.

Another important feature of the "intrinsic" thalamic gliomas was the tendency, in the early part of their life history, to be arrested at the margins of grey or white matter, and the same peculiar self-limitation was also apparent in the case reported by Alfred Meyer. This feature is, of course, not characteristic of the gliomas of the thalamus only; it has been observed in gliomas elsewhere (Scherer, 1936) and in diffuse gliomatosis (Nevin, 1938). In the present cases, however, it is regarded as important because, together with the degree of destruction and degeneration, it indicated the mode of expansion. In all the four cases here reported and in similar cases reported in the literature, the tumour expanded from the neighbourhood of the ventricles in a lateral direction. From these several observations it appears justifiable and useful to regard these four cases of intrinsic thalamic glioma as representing a distinct and well-defined type of intracranial growth.

## Summary and Conclusions.

Six cases of tumour affecting the thalamus (five gliomas and one sarcoma) are described clinically and anatomically and are compared with similar cases already reported.

Thalamic gliomas in a strict sense fall into a well-defined group. Histologically they appear to take origin from the subependymal glial layer and hence they have primary relation to the medial areas of the thalamus, to the caudate nucleus, roof of the mid-brain and to the walls of the lateral ventricles. They invade the brain in a lateral direction, and have little or no tendency to invade the region of the tuber. Clinically they are characterized by the early onset of mental deterioration, and early conjugate ocular palsies. Objective sensory disturbances are absent or

appear only at a late stage of the disease. In the early stage of their development the presence of dementia and iridoplegia may readily suggest general paralysis.

In two cases the thalamus was invaded by tumour from its lateral and ventrolateral aspect. In these, gross sensory disturbances were present at an early stage of the disease.

The differing symptomatology of these two groups may be explained by the location and mode of extension of the tumours: in growths invading the thalamus from the ventrolateral aspect the secondary sensory neuron and its termination are destroyed first; in intrinsic thalamic gliomas which expand from the medial nuclei in a lateral direction the ventrolateral areas of the thalamus are invaded late and incompletely.

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# CORTICAL DEAFNESS WITHOUT APHASIA.

BY W. E. LE GROS CLARK AND W. RITCHIE RUSSELL.

LESIONS of the upper part of one temporal lobe usually produce no disturbance of hearing in either ear. When, however, the auditory cortex of both cerebral hemispheres is diseased complete deafness may result. Cortical deafness, as this condition may be termed, is uncommon owing to the simple improbability of symmetrical lesions occurring in both temporal lobes. Henschen (1918) collected sixteen cases of cortical deafness which up to that date had been reported with *post mortem* examination. Since Henschen's valuable paper, Bramwell (1927) and Misch (1928) have each reported a further case. The case we are here presenting is unlike other recorded cases in that the lesions were both subcortical and were so limited that there was no associated aphasia.

Mrs. F., aged 44, was admitted, under Dr. Hewat's care, to the Edinburgh Royal Infirmary on April 9, 1937. The evening before admission, while sitting in a picture house, the patient had suddenly felt faint and vomited. At the same time she complained of pain in the right side of the head and of loss of power in the left arm and leg. She became dazed, but never unconscious. There had been no previous illnesses of note.

When examined on the day of admission, her face was flushed and she lay in a dazed condition with her eyes closed. She was able, however, to answer questions sensibly and indicated that she had pain in the right parietal region. Ophthalmoscopic examination revealed no abnormality in the appearance of the optic discs or the retinal vessels. The visual fields were normal. The pupils were equal and reacted normally. The ocular movements were full and normal. There was no sensory loss over the face. The facial movements were much less on the left side than on the right. Hearing was good in both ears. The palate moved in the midline, but the tongue was protruded slightly to the left. No movement of the left arm was possible and only very slight movement of the left leg could be made. Apart from some impairment of position sense in the left arm and left leg no sensory loss was detected. The tendon reflexes of the left arm and left leg were more active than on the right side. The left plantar response was extensor, while the right was flexor. The abdominal reflexes were all absent. There was retention of urine. The blood-pressure was 160/90 mm., and the heart was slightly enlarged to the left. The aortic second sound was accentuated. The urine contained no albumin or sugar. There was some vaginal discharge which was found to be free of gonococci. The urea concentration range was: maximum 1·8 mg. per cent.; minimum 0·2 mg. per cent. The blood urea was 27 mg. per cent. The blood Wassermann reaction was negative.

*Progress.*—Catheterization was necessary for six days after admission; thereafter control returned and the strength of the affected limbs improved greatly. She was able to walk a little when discharged on May 7, 1937, for further convalescence. Graduated exercises, massage and occupational therapy were continued, and the condition of the left arm and leg improved. In spite of a low protein diet and treatment with theominal and pacyl, the blood-pressure tended to rise, and on June 14, 1937, was 212/132.

*Second stroke.*—On June 22, 1937, the patient became dazed, incoherent and excited. The breathing became sterterous, but she was not unconscious and could, apparently, recognize people. There was incontinence of urine, but no paralysis was observed, though the patient seemed to be rather spastic. No detailed particulars of the examination on this day are available, but it was noticed that she had some difficulty in speaking for a few hours. The ability to speak and to read correctly quickly returned, but it was soon observed that the patient was quite deaf. She was, therefore, sent back to the Royal Infirmary on June 28, 1937.

When examined on the day of re-admission. the patient had a healthy and alert appearance. All efforts to make her hear were unsuccessful. She could, however, read and write without difficulty, and could speak clearly and correctly in response to written questions. She had no difficulty in carrying out written instructions. In response to written questions she stated that six days previously "I was right enough until after 10 o'clock at night when I began to feel queer and then I couldn't hear anything." She had been quite deaf ever since and had a sensation of loss of feeling in the whole body.

Examination elicited that there was now an extensor plantar response on both sides, whereas when previously in the ward this reflex was abnormal only on the left side. There were, however, no definite signs of weakness or loss of sensation in the right side of the body. The weakness of the left side had largely passed off, but there was still great exaggeration of the tendon reflexes on the left side. Those of the right side were brisker than when previously examined. Examination of the cranial nerves elicited no abnormality. No loss of sensation to pain could be detected.

The above observations allowed the diagnosis of cortical deafness due to bilateral lesions in the temporal lobes of the brain. Dr. I. Simson Hall kindly carried out the vestibular tests and reported as follows:—

The nasal septum is deviated slightly to the right, especially in its upper part; there are no abnormal secretions; the airway is not obstructed. Palatal movements and sensation in the palate are normal. The nasopharynx is healthy. The vocal cords move equally.

*Vestibular functions.*—There is slight initial spontaneous nystagmus to both sides but the movement is not preserved; there is no spontaneous past-pointing error.

*Cold caloric test.—Right ear*: Nystagmus in thirty-five seconds, strong reaction; deviation of the head is very marked; there is a normal past-pointing error.

*Left ear*: Nystagmus in thirty-six seconds. Past-pointing with the left hand is normal; with the right hand there is no error. Nystagmus is horizontal in character.

The patient gives no response with any cochlear function test; she appears to be completely deaf in both ears.

*Progress.*—Though the deafness remained complete, the general condition of the patient improved and she learned to lip-read a little. She was able to walk without much difficulty when she returned home on August 6, 1937.

The patient reported as an out-patient on three occasions during the five months which followed, the last occasion being on January 12, 1938. During this period her condition underwent little change. Her husband said she was easily startled, and there were a few attacks of violent excitement during which several people were required to restrain her movements. Her ability to read, write and speak correctly was demonstrated repeatedly. Her memory was good, both for recent and remote events. A name, address and flower were correctly repeated by the patient five minutes after reading them. The day was given correctly, and simple subtraction was done quite well. When asked if she had pain in her head, she said "no, it isn't a pain, it seems to be a heavy pressing feeling." She said she was unable to hear herself talking, and that there was no improvement in her hearing except that on two occasions she heard a bicycle bell and an alarm clock: she also thought she had once heard some loud singing.

The tendon reflexes remained brisker on the left side than on the right, and the left plantar reflex remained extensor in type. The right plantar response was indefinite. The patient could walk quite well with a stick, but complained that she could not feel the ground with her feet. She also remarked "I can't feel in my body." The exact nature of this sensory disturbance was not ascertained.

Arrangements were made for her re-admission to the ward for further study, but the excitement of leaving home seemed to bring on a pontine hæmorrhage from which she died a few hours after admission on January 22, 1938.

Post-mortem examination was carried out twelve hours after death by Dr. I. G. W. Hill who kindly supplied the following report:—

*General Appearances*:—The body was that of a well developed, well nourished female of middle age. Post-mortem lividity and rigidity present. Serous sacs, pericardial and peritoneal sacs healthy. Pleural sacs: The right showed extensive adhesions binding the right lung to the thoracic wall, which could be divided only with difficulty and were apparently of long standing. The left sac was healthy. Respiratory system: Larynx, trachea and bronchi contained a slight excess of muco-purulent secretion, and the mucosa of the trachea was moderately congested. Lungs of average shape and size, but heavy in consistence and dark red in colour. On section, they were seen to be the seat of marked congestion and œdema, particularly at their bases. Circulatory system: heart of average size and weighed 350 grm. The cavity of the right ventricle was somewhat dilated; that of the left ventricle was normal. There was slight thickening of the muscle of the left ventricle. The endocardium throughout was healthy. The muscle was of a rich brown colour. Coronary vessels healthy. Aorta free from gross atheromatous change.

Alimentary system: Œsophagus, stomach and intestines healthy. Liver of average size, shape and consistence: it was of a rich brown colour and presented no abnormality on section. Gall bladder: bile-ducts and pancreas healthy. Spleen considerably enlarged and weighed 280 grm. It was very soft and, on section, greyish red and diffluent. The appearances were those of reaction to an acute infection. Genito-urinary system: kidneys were somewhat reduced in size and weighed approximately 120 grm. each. They were smooth in outline and somewhat congested in appearance. On section, they showed no obvious pathological change. The capsules stripped readily, leaving smooth, congested surfaces. Microscopically, the kidneys showed no signs of chronic nephritis or of degeneration secondary to vascular disease. Suprarenals healthy. Uterus and appendages: the uterus was moderately enlarged, due to an increase in thickness of the wall. There was no

sign of tumour formation, infection, or recent pregnancy. The ovaries were normal. The thyroid showed slight generalized enlargement and weighed 45 grm.

Brain (we are indebted to Dr. A. C. P. Campbell for the following report): "The calvarium was thick and heavy. The dura was normally adherent to it. The middle ear cavities were healthy. The brain showed considerable gyral flattening of both hemispheres, and marked cerebellar coning. The pons appeared symmetrically slightly enlarged, and on its left ventro-lateral aspect was a hæmorrhagic area where the underlying substance was softened. Apart from the gyral flattening there was no visible external abnormality of the cerebral hemispheres. The leptomeninges were healthy. The basal arteries were transparent and thin, and surprisingly free from atheroma. On section: In each hemisphere an irregular slit-shaped cyst was found deep to the insular cortex: that on the right was the larger; but on both sides the external capsule and claustrum were largely destroyed, with a varying amount of the putamen. On both sides the lesion extended backwards to the level of the pulvinar, and forwards almost to the stem of the sylvian fissure. On each side the acoustic radiation appeared completely transected by the lesion. On the right side the lesion encroached on the lateral surface of the internal capsule in its post-lenticular part. The cortex was not involved on either side. Both these cysts had an irregular tough brown-pigmented wall, and the immediately surrounding brain tissue was of spongy consistence: i.e. they were obviously old ischæmic necroses. It was not possible to say which was the older. A mass of fresh blood-clot was found infiltrating and replacing brain tissue in the left side of the pons and mid-brain, extending upwards into and largely destroying the left cerebral peduncle, the lower part of the left internal capsule and the adjacent ventral part of the left thalamus, including both left geniculate bodies; obviously an apoplectic hæmorrhage of very recent occurrence." The brain was sent to Oxford where the further examination was carried out by one of us (W. E. le G. C.).

### Gross Examination of the Brain

Section of the brain revealed an extensive recent hæmorrhage in the pontine region of the hind-brain, the cause of the patient's death on January 22, 1938. The hæmorrhage was situated in the dorsal region of the left side of the pons, extending up into the centre of the left cerebellar hemisphere, into the tegmental region of the left side of the mid-brain, and also into the ventral half of the left thalamus involving here the ventral thalamic nucleus and the pulvinar. The 4th ventricle was filled with recent clot. The 3rd and lateral ventricles were normal except for a very moderate distension.

In the cerebral hemispheres, the sites of the lesions associated with the strokes which occurred on April 9 and June 22, 1937 (as the result of which cortical deafness supervened) are marked by a bilaterally symmetrical cavitation in the external capsule. The cavities are lined by a yellow membrane which was found histologically to contain abundant macrophages filled with granules of blood pigment. On each side the cavity corresponds almost exactly in its extent with the cortex of the insula (figs. 1 & 2). Rostrally (fig. 2*a*), it is limited to the white matter of the ventral half of the external capsule between the lentiform nucleus and the claustrum. In the middle of its extent (fig. 2*b*) it is broader, involving the greater part of the claustrum except for its dorsal extremity, and the ventro-lateral part of the putamen of the lentiform nucleus. At its caudal extremity (fig. 2*c*), which corresponds closely in level with the caudal limit of the insula, the lesion is again confined to the white

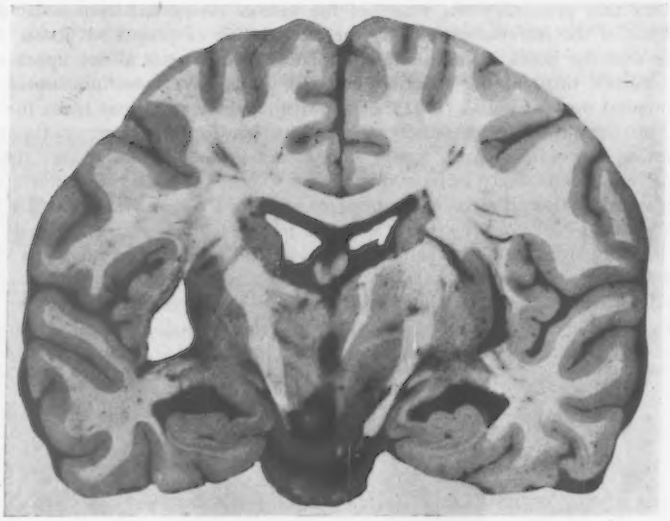

FIG. 1.—Transverse section of the fresh brain showing the bilateral lesions in the external capsule.

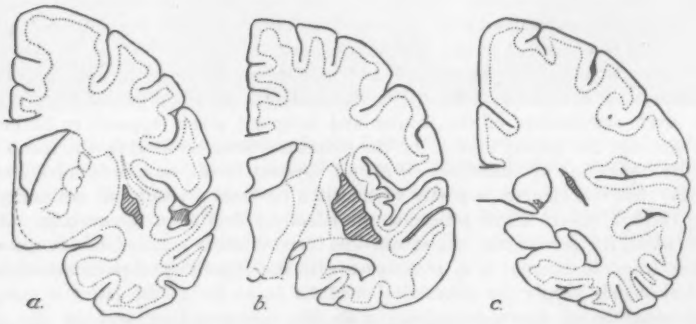


FIG. 2.—Tracings of transverse sections through the right cerebral hemisphere at the level of (*a*) the anterior extremity, (*b*) the middle, and (*c*) the posterior extremity of the lesion in the external capsule. Note that the lesion involves only the ventrolateral portion of the putamen of the lentiform nucleus, while the globus pallidus remains intact. × ½.

matter. From the position of the lesion, as shown on macroscopical examination, it is clear that practically the whole of the insular cortex has been isolated from the region of the internal capsule by the interruption of projection fibres. It also appears that the fibres of the auditory radiations which pass to the upper surface of the middle third of the superior temporal gyrus have been interrupted. The experimental work of Poliak (1932) has shown that these radiations reach the cortex partly by coursing immediately ventral to the lentiform nucleus, and partly by penetrating its ventral part. Lastly, the dorsal margin of the lesion reaches a position where it is likely to have interrupted some of the projection fibres related to the ventral extremities of the central convolutions. It is clear that the lesions in the external capsules must have been the result of a bilateral thrombosis of the most laterally situated of the basal branches of the middle cerebral artery.

*Histological examination.*—Owing to the damage done to the thalamus on the left side of the brain by the hæmorrhage which occurred just before death, histological studies were confined to the right side. Sections through the site of the lesion were prepared by the Weigert-Pal method, and others were stained with

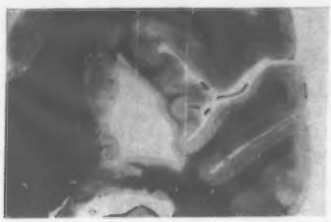

FIG. 3.—Transverse section through the middle of the lesion in the right cerebral hemisphere stained by the Weigert-Pal method. Natural size.

toluidin blue. Serial transverse sections were also made through the caudal half of the thalamus and stained with toluidin blue in order to study the cellular degeneration related to the lesion in the external capsule.

Weigert sections (fig. 3) confirm the infcrences drawn from the macroscopic appearance of the lesion in regard to the involvement of projection fibre systems. The myelo-architecture of the insular and temporal cortex appears to be normal. The fact that the greater part of the claustrum has been involved by the lesion bears out the contention of Shellshear (1920) (as opposed to the statements of Duret and Beevor) that this element is partly vascularised by basal arteries and not entirely by deep cortical vessels which penetrate the island of Reil from the surface. On the other hand, the persistence of a subcortical layer of white matter beneath the island of Reil (capsula externa) is in accordance with the experimental demonstration that cortical vessels supply the subcortical medulla in so far as the latter is composed predominantly of fibres connecting with the corresponding area of the cortex (Sunderland, 1938).

While the Weigert sections give no indication of the extent of the cortex in the middle third of the superior temporal convolution whose fibres have been interrupted by the lesion, the toluidin blue material does provide evidence on this point, since the track of the degenerated fibres is marked out by a zone of gliosis (fig. 4*a*). From

this it appears that only the fibres passing to the upper surface of the cortex have been involved. Since the lesion resulted in complete cortical deafness, it may be assumed therefore that the audito-sensory area is confined to the upper submerged surface of the middle third of the superior temporal convolution (i.e. the transverse gyri of Heschl). The auditory projection area of the medial geniculate body thus

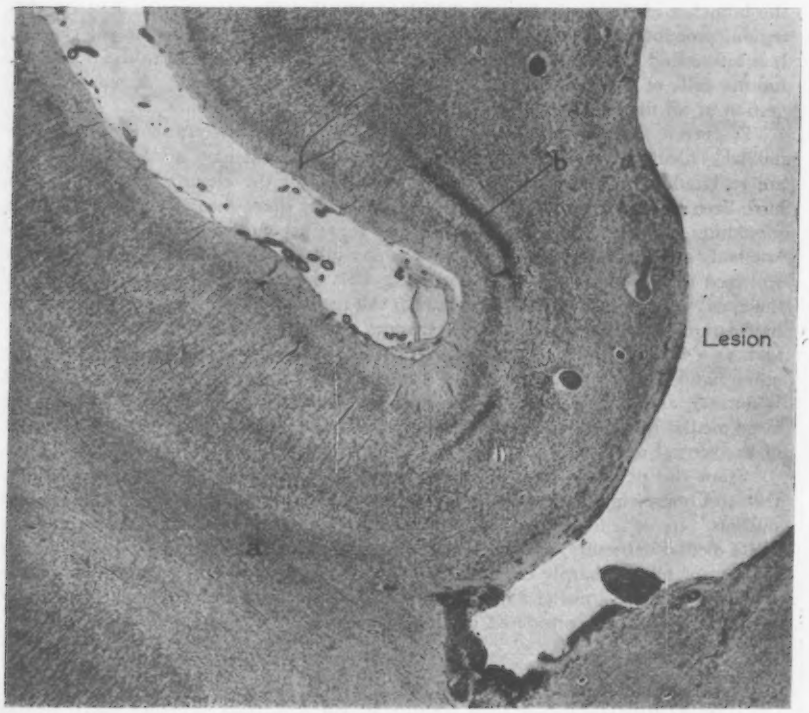


FIG. 4.—Transverse section through the lower margin of the lesion on the right side, stained with toluidin blue. Note the zone of gliosis (*a*) which marks the track of degenerated fibres of the auditory radiations passing to the upper surface of the superior temporal gyrus, and the small area of hæmorrhage (*b*) which affects the internal granular layer of cortex at the junction of the lower margin of the island of Reil with the superior temporal gyrus.

appears to be considerably more limited than some of the older neurologists supposed. Dejerine, for example, believed that the auditory radiations end in the whole of the superior temporal convolution, while, according to v. Monakow, they extend also to the second temporal convolution. However, recent experimental work on monkeys has demonstrated how small relatively the auditory area is in the Primate brain (Clark, 1936: Walker, 1937).

The toluidin blue sections show that the cyto-architecture of the insular and temporal cortex is quite normal with the exception only of a small area at the junction of the two. Here there is a curious vascular lesion limited to the internal granular layer of the cortex (fig. 4*b*). The granule cells have completely disappeared and are replaced by a proliferation of small blood-vessels and numerous macrophages filled with blood pigment. This can only be due to minute hæmorrhages involving the branches of the cortical vessels which supply the internal granular layer in this region, probably as a secondary result of the hæmorrhage in the external capsule. It is interesting to note, however, that the cortical lesion is confined to the one layer, for the cells of the supra- and infra-granular layers are normal. A marked congestion of all the cortical vessels in this zone, however, is evident.

The serial sections through the thalamus show some interesting features. The medial geniculate body is completely degenerated: its cells have all disappeared and are replaced by a conspicuous gliosis. Moreover, all the elements of the nucleus have been involved, including the large cells in the dorso-medial region which are sometimes included under the term nucleus supra-geniculatus. The lateral geniculate body appears to be normal; if there is any cell atrophy in this element, it is too scattered and insignificant to be detected. Cell degeneration has also occurred in the small intergeniculate nucleus (between the medial and lateral geniculate bodies), in the most ventral portion of the pars externa and pars arcuata of the ventral nucleus, and, to a limited extent, in the lateral and central areas of the pulvinar. On the other hand, the cyto-architecture of the posterior projecting pole of the pulvinar is normal, and this is also the case with the lateral nucleus of the thalamus, the large medial (dorso-medial) nucleus, the parafascicular nucleus, and the greater part of the ventral nucleus.

From the point of view of the cortical connections of the thalamus, perhaps the most interesting observation is the almost total degeneration of the centre median nucleus. Its cells have completely disappeared except for an insignificant number at its medial extremity, and the space which it normally occupies is marked out by an area of gliosis sharply circumscribed above and laterally by normal cells of the medial and ventral nuclei and medially by the parafascicular nucleus. This effect of the lesion will be considered in another paper.

## Conclusions.

The symmetrical vascular lesions in the external capsules have neatly isolated on either side the insular cortex, and the submerged cortex of the upper surface of the middle third of the superior temporal convolution. In addition a small proportion of the projection fibres connected with the lower extremities of the central convolutions was probably involved. In relation to these cortical lesions, an examination of the thalamus shows complete cell degeneration in the medial geniculate body, the intergeniculate nucleus, and the centre median nucleus. There is also a partial cell degeneration in the most ventral portion of the ventral nucleus and in the base of the pulvinar. The complete degeneration of the medial geniculate body is related to the cortical deafness which supervened when the vascular lesion in the external capsules occurred.

In addition to the acknowledgements already made, we are grateful to Dr. A. Fergus Hewat and to Dr. R. H. Thomson, Uphall, for kind permission to investigate the case under their care, and for their cordial assistance.

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# CEREBRAL SUBCORTICAL MYELINOPATHY IN CARBON MONOXIDE POISONING.

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BILATERAL softening of the anterior part of the globus pallidus has been regarded as pathognomonic of carbon monoxide poisoning and used even for medicolegal purposes. The other acute and chronic changes in the brain described, though not so regular and typical, are thickening of the meninges, œdema, hyperæmia, miliary hæmorrhages, arteriosclerosis, endarteritis, thrombosis, embolism, softenings in the cerebral cortex, cornu Ammonis, zona reticularis of the substantia nigra and cerebellum, degenerative proliferative changes in the medulla, profuse glial proliferation and patches of demyelinization in the deeper cerebral white substance, cell destruction in the anterior horns of the spinal cord, and neuritis of the peripheral nerves. Compared with the extensive discussion of the pathology of the basal lesions, the diffuse reaction in the deeper white substance has been reported relatively seldom. Sayers and Davenport (1930) made a very thorough review of the literature up to 1930. Thereafter the scattered reports of various authors added few new ideas, but tended rather to favour multiple factors of the pathogenesis of this malady. In brief the various theories may be mentioned under the following categories: (1) direct action of the gas on the tissue (Gleister quoted by Mayers (1927), Dreser quoted by Meyer (1928), Mathews (1920), and Haldane (1927)); (2) a special physicochemical affinity of certain parts of the brain (pallidum) for the gas (Vogt, C. and O. (1922); (3) anoxæmia (Strecker, Taft and Willey (1927), Henderson (1916), Haldane (1895), Beck (1936), Walters (1927), Haggard (1922), and Yant, Chornyak, Schrenk, Patt and Sayers (1934)); (4) organic changes of the blood-vessels (Sayers and Davenport (1930), and Hill and Semerak (1918)); (5) functional disturbances of the blood circulation (Meyer (1928), Klebs (1865), and Hiller (1924); (6) anatomical peculiarities and special arrangement of the blood supply to the basal ganglia (Kolisko (1893), and Poelchen (1888)); (7) a multiple factor (Stewart (1920), Gordon, Taylor and Margolies

(1932), Delafield and Prudden (1922), Grinker (1925), (1926), and (1934), and Hassin (1933)). Except for the last, practically none of these theories has been free from serious objection. The possibility of direct action of the gas on the tissue was excluded by the experiment of Haggard (1922). The theory of anoxæmia was supplemented by Mathews (1920), Lewin (quoted by Sayers and Davenport (1930)), Stadie and Martin (1925-26), Warburg (1926), Keilin (1928-29), Campbell (1929-30), and others, and doubted by Gippert (quoted by Stewart (1920)), and others. The theory of special pathoclisis can neither explain the frequent involvement of the neighbouring internal capsule nor that of the distant parts of the nervous system, nor the particular selection of the anterior portion of the pallidum, nor the similar symmetrical lesions of a totally different ætiology (Weimann (1926), and Rotter (1929)), nor the absence of permanent lesions in chronic carbon monoxide poisoning (Grinker (1925) and (1926)). Similarly the idea of local anatomical anomaly is inadequate, though it explains better the particular affection of the anterior portion of the pallidum. The organic changes of the blood-vessels cannot be demonstrated constantly. The theory of functional disturbances of the blood circulation seems very sound, but again it fails to answer the question of predilection of the lesions for the basal ganglia. Since none of the individual hypotheses is without defect, a multiple view-point would naturally arouse the sympathy of most advocates. At present the most acceptable view is that which invokes the physiological factors of anoxæmia, and of vascular disturbance, and the anatomical factor of peculiar blood supply.

In a small series of three cases with autopsies observed here, one showed typical bilateral hæmorrhagic softening in the globus pallidus with no significant changes in the white matter, and two presented diffuse changes in the deeper cerebral white substance, one of which was under the care of Dr. C. S. Yang, of Hsiang Ya Medical College, Hunan. Since two of three cases show a pathological picture which is not of the ordinary type, we feel it worth while to report them here.

*Case 1.*—Male, aged 40. Early in the morning, eight days before admission, the patient, a perfectly healthy man, was found lying unconscious in a cave just in front of a big stove. Consciousness returned twenty-four hours later and he resumed his usual activity, attending the stove for the next four days without any symptom. From the sixth day on he suddenly became excited and restless and showed much odd behaviour. His speech was slurred and his upper extremities tremulous. Very soon he became semiconscious and showed a generalized rigidity. He uttered no words, took no food or drink by himself, voided and defæcated on the bed without control. On admission he was found to be in a drowsy state with evidence of moderate dehydration. His eyes remained closed most of the time but could be opened in response to stimulus. He refused to reply to any question.

His neck was retracted. All extremities, including the hands, were held in flexion and were resistant to manipulation. Their rigidity was so great that they returned spontaneously to the original flexed position as soon as the counter-force in extension was released. To open his mouth was impossible. There was constant profuse perspiration over the face. The tendon reflexes were equally increased on both sides. The abdominal reflexes were not obtained. No clonus or Babinski sign could be demonstrated. The pupils were active to light. The fundi showed mild papillœdema. Hearing seemed not to be seriously affected, if at all. Sensibility to pin-prick was preserved throughout the whole body. Sudden jerky movements of the eyelids, nose and mouth were frequently noticed. Further neuropsychiatric examination could not be made. The chest and abdomen were essentially normal. The body temperature, pulse, respiration and blood-pressure were all within normal limits. Examination of the blood, urine, stool and cerebrospinal fluid gave negative information. The Wassermann reaction of both blood and cerebrospinal fluid was negative. Analysis of the blood for carbon monoxide by the gasometric method of Van Slyke and Neill revealed no detectable amount. During his stay in the hospital for forty-nine days he showed practically no change in his general condition. Hypodermic injections of atropine and electrolysis with magnesium chloride over the orbits produced no persistent influence upon the generalized rigidity. After discharge his condition became steadily worse and he died quietly about four months after the poisoning.

The body was immediately embalmed following death by injection of formalin into the femoral artery and the cisterna magna. Autopsy was done four months later.

The brain and the spinal cord were well fixed and normal in shape, size and consistency. The brain showed a diffuse shrinkage of the gyri. The meninges were thin and free from exudate and hæmorrhage. The pial and basal vessels showed no abnormality. Frontal sections revealed congestion of all the small blood-vessels. The caudal part of the thalamus on both sides and the interpeduncular region of the mesencephalon were of a slight darkish brown colour. The ventricles were not dilated. There was no hæmorrhage or thrombosis throughout. The spinal cord was essentially normal.

The histological changes were confined principally to the cerebral white matter, being pronounced locally at the internal capsule and the anterior commissure. A great abundance of "gemästete" glia and a moderate amount of "gitter" cells and hypertrophied microglia (red cells) were noticed throughout the deeper cerebral white matter with the exception of a narrow zone immediately below the cortical grey layers (U-fibres) (fig. 1). The distribution of the proliferative changes was diffuse and tended to be arranged in a certain pattern in relation to the engorged blood-vessels. The "gamästete" glia lay immediately next to the vessels; the "gitter" cells tended to be situated in an outer zone; and the rod cells were scattered at the periphery. Some of the blood-vessels showed deposition of greenish pigments on their walls.

Spielmeyer's myelin-sheath method revealed in the deeper white matter confluent patches of demyelinization with swelling of the sheaths and the formation of balls (fig. 2). The U-fibres were intact. The Scharlach R stain showed numerous lipoid globules arranged in a similar manner which appeared bright red at the centre and brownish yellow or orange at the periphery (fig. 3). However, a clear-cut relationship to the blood-vessels could not be demonstrated by either of these

PLATE XX.

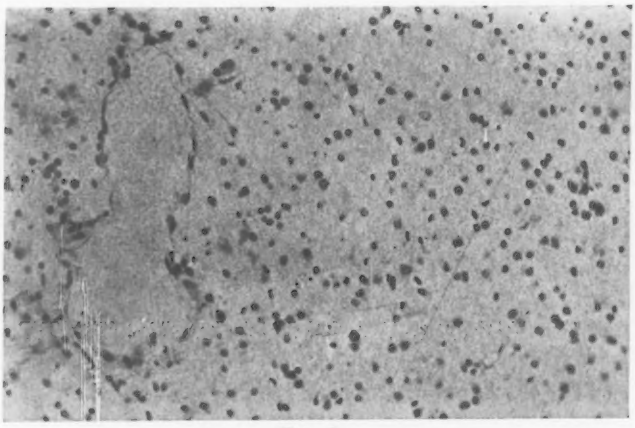

FIG. 1.

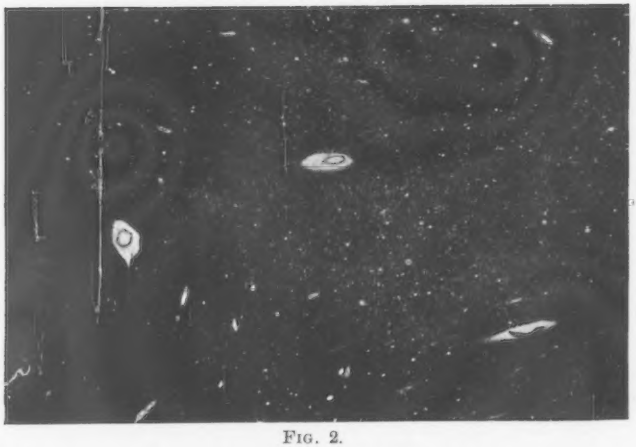

FIG. 2.

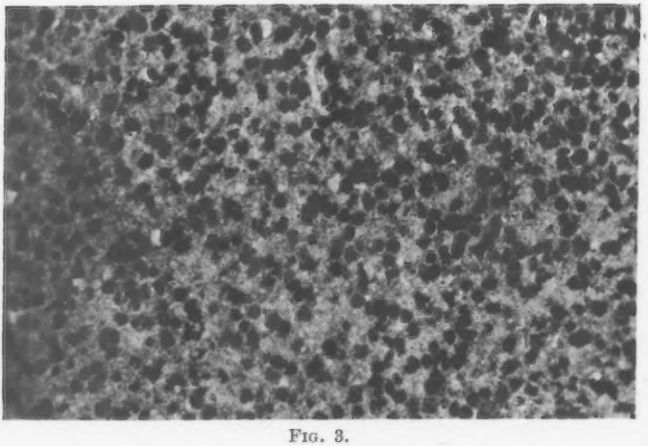

FIG. 3.

*To illustrate article by Y. K. Hsü and Y. L. Ch'eng.*

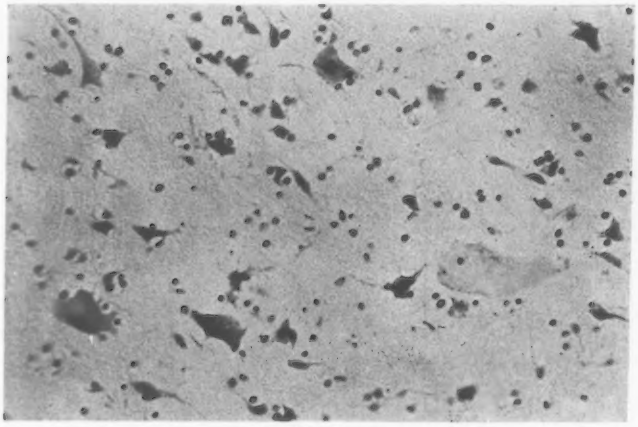

FIG. 4.

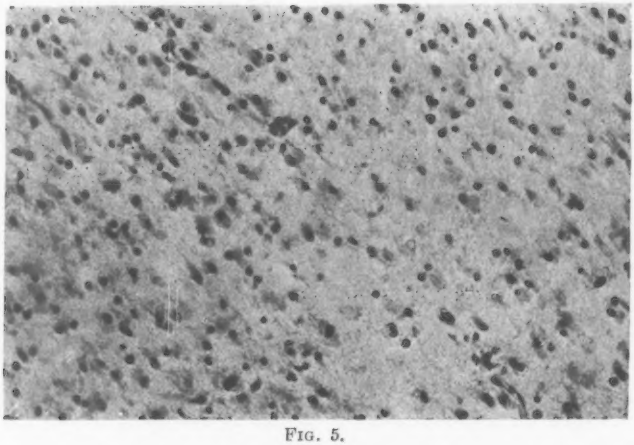

FIG. 5.

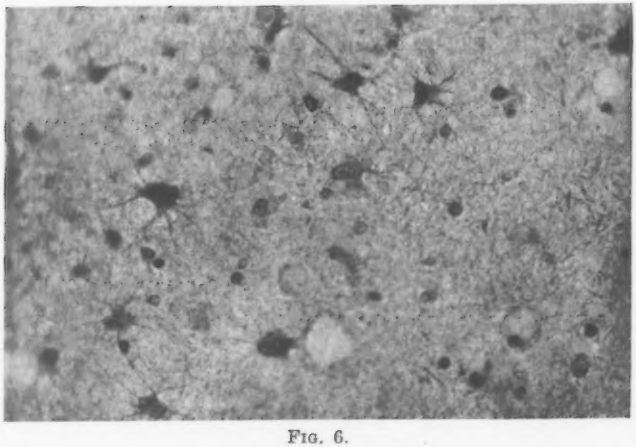

FIG. 6.

*To illustrate article by Y. K. Hsü and Y. L. Ch'eng.*

special stains. Many fibrous glia cells were shown by Holzer's method. The axis cylinders were diminished in number and slightly thickened with the occasional formation of balls.

Some of the ganglion cells in the third and fifth cortical layers appeared to be pale and swollen with the granular nucleus pushed to the periphery and the processes visible for a distance (fig. 4). The meninges were normal. There was no hæmorrhage or thrombosis.

Section through the left basal ganglia at the level of the anterior commissure showed disperson of "gitter" cells and "gamästete" glia in the corpus striatum, pallidum, internal and external capsules, and anterior commissure. These progressive changes were much more pronounced in the white substance than in the grey nuclei. The "gamästete" glia tended to be arranged around the blood-vessels, especially around those in the white matter near the border of the caudate nucleus. The special stains for myelin sheaths, fat, glial fibres and axis cylinders revealed a similar picture to that of the cerebral white substance. A tiny glial scar composed of "gitter" cells, fibroblasts and glial fibres was noticed at the inner border of the pallidum just adjacent to the internal capsule. No such lesion could be demonstrated in the corresponding right pallidum. The ganglia cells, except in the scar, were rather well preserved. The blood-vessels, especially in the caudate nucleus, showed slight lymphocytic infiltration of the adventitia.

The cerebellar white substance showed changes similar to those in the cerebrum, but they were much less marked than the latter.

The thalamus, mesencephalon, pons, medulla oblongata and spinal cord were essentially normal.

*Case* 2.—Male, aged 49. After sleeping one night in a closed room with a stove, the patient was discovered unconscious the next morning. Muscle-tone was increased, particularly in the right upper extremity. The condition gradually improved so that two days later he regained consciousness. Some râles were heard at the lung bases. While the general condition showed no change, there was definite evidence of extension of a pneumonic process in the left chest one week later. He suddenly appeared very ill and drowsy after another week and his temperature rose for the first time. Findings by this time suggested empyema of the left pleura and aspiration yielded thin pus from which the pneumococcus was grown. Then incontinence of urine and fæces set in and muscle-tone was further increased. Lumbar puncture yielded essentially normal cerebrospinal fluid. Following a short period of slight improvement the patient became much worse and died four weeks after the accident.

The post-mortem examination was limited to the brain. The brain appeared normal in shape, size and consistency. The meninges were slightly congested and showed a few small specks of thickening. The basal arteries showed no evidence of atheromatous changes. Frontal sections revealed slight congestion of the small blood-vessels, but were otherwise not remarkable. The globus pallidus on either side looked normal. The ventricles were not dilated. There was no gross hæmorrhage or thrombosis.

Throughout the entire cerebral cortex from the frontal to the occipital poles extensive changes were seen in the white matter. Only a narrow zone lying immediately underneath the cortical grey matter (U-fibres) appeared unaffected. In Nissl preparation there was a marked proliferation of the glial cells with

numerous " gemästete " glia and " gitter " cells (fig. 5). These changes were especially pronounced around the blood-vessels and seemed to be arranged in a pattern similar to that in the first case. The blood-vessels were engorged and showed marked distension of their perivascular spaces, some of which were filled with pigment-loaded phagocytes. The vascular endothelium was, however, normal.

With Scharlach R stain, diffusely scattered fatty granule cells were seen with no special reference to the blood-vessels. With Spielmeyer's myelin sheath stain many of the " gitter " cells contained granules stained with hæmatoxylin and the picture was very uneven, with irregular thinning of the myelin sheaths. With Holzer's stain the fibrous astrocytes could be easily demonstrated (fig. 6).

Section of the anterior part of the basal ganglia revealed similar changes in the globus pallidus and all the white substance, including the internal and external capsules, fornix and anterior commisure. They were most marked in the internal capsule, less in the fornix and pallidum, and least in the external capsule and anterior commissure. Small fresh perivascular hæmorrhages were seen in the corpus striatum.

The cerebellum showed exactly the same change in the white matter as did the cerebrum.

A similar but less pronounced proliferation of glia cells was shown in the pes pedunculi, particularly the regions adjacent to the substantia nigra and the medial and lateral portions of the pes.

The meninges over the cerebral cortex were in places slightly thickened and infiltrated with a few large mononuclear cells. The pial vessels were normal. The small blood-vessels in the cortical grey layers were engorged, but otherwise not remarkable. The ganglion cells throughout the brain appear to be preserved. There was no evidence of inflammatory changes.

The pons and medulla oblongata showed no findings of significance.

## Discussion.

In regard to the diffuse reaction in the deeper cerebral white substance caused by carbon monoxide poisoning, the observations of Hiller (1924), Grinker (1925, 1926 and 1934), Meyer (1928), Stewart (1920), Strecker, Taft, and Willey (1927), and Yant, Chornyak, Schrenk, Patty and Sayers (1934), deserve special consideration. It is, in fact, not so rare as reported and ought to be considered by no means less pathognomonic than bilateral softening of the globus pallidus. Ordinarily such a process is concomitant with the basal lesions and it is generally believed to be due to a severe alteration in myelin which was labelled by Grinker as myelinopathy. In our cases the lesions are principally the same as in theirs, but the absence of symmetrical softening in the pallidum is of extraordinary interest. This is in accord with Meyer's observations that the same independent change in the white matter may take place both in human cases and in animals. Obviously one should keep in mind the fact that affection of the pallidum is not necessary, in order not to miss recognition of the disease at the time of post-mortem examination.

As to the pathogenesis of the outstanding changes in the central nervous system the view of Grinker seemed to be the most adequate so far. He believed that carbon monoxide causes anoxæmia, and that vascular paralysis renders the anterior pallidum with its peculiar blood supply and the deeper white matter with its meagre capillary network relatively susceptible to destruction. But how does this explain those cases with independent changes, either in the basal ganglia, or in the white matter? How is this variation of distribution related to the duration of disease, the severity of poisoning, the personal susceptibility to the gas and the pre-existence of abnormalities in the brain ? To these questions no one can as yet formulate a definite answer. From our present observation we can postulate two possible mechanisms by which the degeneration of the white matter may occur. In case of an indirect effect of the poison through the disturbance of the circulation we should expect to find foci of necrosis in distinct relationship to certain vessels, or a more pronounced degree of degeneration in the district of a particular blood supply. In our preparations lesions of such a nature are absent. Then we have to think of a direct effect of the poison on the white substance in which case we should naturally expect to see a more or less immediate and diffuse reaction of the same age in the different parts of the nervous system. In contrast to Meyer's findings our cases show more of the nature of a direct toxic action to the white matter, either by the poison itself or by its anoxæmic effect. This being so, the metabolism of the nerve fibres or myelin sheaths is deranged and their nutrition becomes inadequate leading eventually to progressive degeneration of their structure.

In our first case the tiny glial scar in one pallidum certainly suggests the existence of a previous small necrosis. It is, however, only one-sided. The peculiar change in the ganglion cells is not unlike that described by Merritt and Springlova (1932), in Lissauer's dementia paralytica and by Williams (1935), in all kinds of degenerative changes in the subcortical white matter. Perhaps it did not result directly from the carbon monoxide poisoning, but it suggests an axonal reaction secondary to the lesions in the white matter. This is also the opinion of Williams. The infiltration of the adventitia of the vessels in the corpus striatum strongly suggests a symptomatic process.

In our second case, the significance of fresh diapedesis in the corpus striatum should not be over-emphasized. It is very unlikely that it is a sign of hæmorrhagic softening.

Clinically these two cases belong to the so-called relapsing type; that is, secondary changes appeared after recovery from the initial disturbances (Beck (1936), Borman (1926), Dancey and Reed (1936), and McConnell and Spiller (1912)). The interval of freedom is apparently due to the slow

development of the pathological process in the brain which must reach a certain degree before producing symptoms. The picture of catatonia and Parkinsonism presented by our first case has been repeatedly described in carbon monoxide poisoning, and generally ascribed to a diffuse change in the white matter in respect of the psychic symptoms, and to the basal lesions in respect of the general rigidity (Strecker, Taft and Willey (1927), Meyer (1928), Stewart (1920), Gordon, Taylor and Margolies (1932), Grinker (1925, 1926 and 1934), and Dancey and Reed (1936)). From our observations it seems that both the neurological and the psychic symptoms can be accounted for by the severance of the connecting fibres between the cerebral cortex and the centres at a lower level. The absence of mental manifestations in our second case and the partial recovery from neuropsychiatric symptoms in Borman's (1926) suggest strongly that there is a lack of strict correlation between the appearance of mental disorder and the extent of anatomical lesions in the brain. The former seems to be related more closely to the individual constitution than to the duration of the disease and severity of the damage.

Since the fine lesions in carbon monoxide poisoning are often multiple and diffuse and may attack any portion of the nervous system, the symptoms may simulate many nervous and mental diseases (Beck (1936), Gordon, Taylor and Margolies (1932), Hassin (1933), Dancey and Reed (1936), and Wolff (1926-27)). Although pictures of catatonia and Parkinsonism are encountered more frequently than other syndromes, yet the finding of a diffuse reaction in the deeper white matter is of no less significance than that of basal lesions.

SUMMARY.

(1) Two "relapsing" cases of carbon monoxide poisoning with post-mortem examinations are reported.

(2) One patient presented symptoms of catatonia and Parkinsonism and died four months after the poisoning. The other developed early in the course bronchopneumonia and empyema, and died four weeks later.

(3) Both brains showed a more or less diffuse degeneration of the white matter with marked progressive changes of glia cells and patches of demyelinization. There was no bilateral softening of the globus pallidus.

(4) A direct influence of the poison, or its anoxæmic effect on the nervous tissue, is emphasized as an outstanding pathogenetic factor for our cases, in addition to the acceptance of Grinker's view.

(5) The discrepancy between the symptomatology and the extensiveness of the lesions is worthy of note.

(6) Attention is called to the significance of the changes in the deeper white matter in carbon monoxide poisoning.

We wish to express our great indebtedness to Professor W. Scholz for advice and encouragement in the preparation of this report and to Dr. C. S. Yang for allowing us to examine the brain of his patient.

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## LEGENDS FOR PLATES.

FIG. 1.—*Case 1.* Frontal section showing proliferative changes of the glia cells in the white matter. Nissl stain × 220.

FIG. 2.—*Case 1.* Frontal section showing patches of demyelinization in the white matter. Spielmeyer's stain × 16.

FIG. 3.—*Case 1.* Frontal section showing numerous lipoid globules in the white matter. Scharlach red stain × 100.

FIG. 4.—*Case 1.* Motor cortex showing peculiar change of a large pyramidal cell. Nissl stain × 220.

FIG. 5.—*Case 2.* Occipital section showing proliferative changes of the glia cells in the white matter. Nissl stain × 220.

FIG. 6.—*Case 2.* Frontal section showing increase of fibrous astrocytes in the white matter. Holzer's stain × 295.

# OLFACTORY ALLOÆSTHESIA.

BY JOHN D. SPILLANE.[1]

During the course of investigations of olfactory function in brain tumours, using the method recently described by Elsberg (1935), it was repeatedly observed that certain patients referred an odour injected into one nostril to that of the opposite side and failed to detect the odour on the side of injection. At first glance such a phenomenon might appear to be of little significance, merely suggesting a crossing of the stream of odour in the nasal passages or nasopharynx. However, special attention to the occurrence suggested that such was probably not the explanation. In this paper these observations are recorded and an explanation offered for the phenomenon.

The apparatus used and the principles on which tests of olfactory function were made have been fully described in previous papers (Elsberg, Brewer and Levy, 1935 and 1936) and only a short summary of the method will here be given.

Two tests are made: the blast injection and the stream injection tests. The former is made on the principle of the injection of a known volume of odour into one nostril during a period of voluntary apnœa. The apparatus consists of a test bottle of fixed size containing a known quantity of odorous substance (coffee or citral) and fixed with an inlet and an outlet tube. A known volume of air is injected into the bottle from a syringe and released into one nostril during a period of voluntary apnœa. The number of c.c. of odour that have to be released into one nostril in order that the odour be identified is termed the minimum identifiable odour (M.I.O.). The stream injection is used for the study of olfactory fatigue. A stream of air of known rate is passed from a tank of compressed air through the test bottle and thence to the nostril. Blast injections of the M.I.O. are then made into that nostril at thirty-second intervals, and the time that elapses before the odour is again identified is measured.

In twelve out of some ninety-two cases of suspected brain tumour examined by these methods, it has been observed that for a short period following the stream injection into one nostril, subsequent blast injections

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of the M.I.O. into that nostril were referred to the opposite side and not appreciated on the side of injection. In some cases this transference persisted for ten or twelve minutes following the stream injection. In each case it was observed that transference occurred in only one direction. For instance, in Case 1 (*see* table) blast injections into the right nostril following a stream injection into that nostril, were unhesitatingly identified as coming from the left nostril; but all odours injected into the left nostril, before and after a stream injection into that nostril, were readily localized to that side. The observations made on the twelve patients are summarized in what follows.

(1) In three of the twelve cases transference of odours was found on simple blast injections *before* the nostril on that side had been subjected to the stream injection.

(2) In a few instances, a doubtful case of transference before fatiguing with the unilateral stream injection, was converted into a well-marked phenomenon by administering the stream injection.

(3) In some instances the odour was correctly lateralized if, instead of blast injections of the M.I.O. being made, larger quantities were used. Thus, when a blast injection of the threshold stimulus, say of 8 c.c., was appreciated in the *other* nostril, an injection of 30 c.c. could be detected on the *correct* side.

(4) The phenomenon persisted for several minutes following the stream injection. In the majority of cases correct lateralization became re-established after six or ten minutes. (*See* table.)

(5) In eleven of the twelve cases the phenomenon was observed for both coffee and citral. In one it was present for coffee alone and was found to be inconstant for citral.

(6) Injections of air did not produce the phenomenon in these individuals. A blast of air, when appreciated, was never consistently referred to the opposite side.

(7) In ten of the twelve cases, the minimum identifiable odour and the duration of olfactory fatigue were within normal limits. The phenomenon of transference was the only abnormality.

(8) In a series of ninety-two individuals, normal or suffering from some form of nervous disease, only the twelve recorded instances were observed. The normal individual nearly always correctly lateralized the side of stimulation or else expressed doubt concerning the matter. He never consistently referred the stimulus to the opposite side while failing to identify it on the side of injection.

(9) In nine of the twelve instances of transference of the olfactory

stimulus, a cerebral tumour was found on the side on which the odour could not be detected. Thus, in a left-sided tumour such as Case 2, blast injections of the M.I.O. on the left side, following a stream injection on that side, were appreciated as originating in the right nostril, while no odour was detected in the left. A transference occurred from the diseased to the healthy side. In three instances, however, Cases 6, 9, and 10, the

OLFACTORY STUDIES IN TWELVE BRAIN TUMOURS.

| Case | Verified diagnosis | M.I.O. | | | | Fatigue in mins. | | | | Duration of transference | | Direction of transference |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Coffee | | Citral | | Coffee | | Citral | | Coffee | Citral | |
| | | R. | L. | R. | L. | R. | L. | R. | L. | | | |
| 1 | Rt. frontal astrocytoma | 4 | 5 | 4 | 5 | 0 | 1·5 | 2 | 2 | 5 min. | 5 min. | R. → L. |
| 2 | Lt. frontal meningioma | 8 | 9 | 3 | 6 | 2 | 2 | 2 | 0 | 5 „ | 4 „ | L. → R. |
| 3 | Lt. frontal glioblastoma | 19 | 5 | 13 | 5 | 2 | 2 | 2 | 0 | 6 „ | Nil | L. → R. |
| 4 | Lt. frontal astrocytoma | 5 | 8 | 5 | 8 | 1 | 1 | 6 | 1 | 7 „ | 6 min. | L. → R. |
| 5 | Lt. frontal glioblastoma | 6 | 7 | 8 | 8 | 2 | 2 | 1 | 4 | 7 „ | 8 „ | L. → R. |
| 6 | Rt. frontal glioblastoma | 6 | 8 | 4 | 6 | 2 | 3 | 2 | 0 | 12 „ | 11 „ | L. → R. |
| 7 | Lt. parietal tuberculoma | 8 | 7 | 6 | 4 | 1 | 1 | 1 | 0·5 | 4 „ | 3 „ | L. → R. |
| 8 | Rt. fronto-temporo-parietal glioblastoma | 12 | 8 | 11 | 7 | 0 | 0 | 0 | 0 | 9 „ | 10 „ | R. → L. |
| 9 | Rt. fronto-temporal astrocytoma | 11 | 8 | 18 | 6 | 3 | 0 | 6 | 0 | 8 „ | 8 „ | L. → R. |
| 10 | Rt. acoustic neuroma | 11 | 10 | 6 | 5 | 0 | 5 | 1 | 1 | 13 „ | 10 „ | L. → R. |
| 11 | Lt. acoustic neuroma | 22 | 8 | 10 | 7 | 1 | 2 | 1 | 5 | 10 „ | 10 „ | L. → R. |
| 12 | Lt. cerebral neoplasm | 13 | 8 | 17 | 17 | 8 | 6 | 5 | 5 | 8 „ | 8 „ | L. → R. |

tumour was situated on the side to which the odour was incorrectly thought to have been applied. In these three cases transference was definite for both coffee and citral, and persisted for 12½ minutes, 8 minutes, and 13 minutes, respectively. Cases 9 and 10 were tumours of the acoustic nerve, arising in the cerebellopontine angle, and giving rise to hydrocephalus.

## Discussion.

The first possible explanation for the occurrence of the phenomenon is that some, or all, of the injected odour crosses to the other side in

the nasal passages or nasopharynx. There are several reasons why this explanation is improbable.

(1) There was no history of injury to the nose and no deformity of the nasal passages in any of the recorded cases.

(2) If the odour crossed in the nasal passages or nasopharynx there would be no good reason why transference in any one individual always occurred in only one direction. If the odour crossed in the nasal passages, one would expect to see it occurring in both directions; namely, from right to left *and* from left to right. Again, there would be no explanation why *all* the odour should cross and *none* be appreciated on the side of injection.

(3) In paragraph (3) above, it was shown that in some instances the odour was correctly lateralized if larger quantities were used instead of threshold amounts that were only appreciated in the opposite nostril. Such a condition could hardly arise if transference were taking place in the nasal passages.

(4) Two individuals with pituitary tumours (who did not show the transference phenomenon) with anosmia on one side and normal olfactory acuity on the other side, provided interesting experimental conditions. In one case the growth had been removed by transfrontal approach with injury to the olfactory nerve on that side, resulting in anosmia. In both these individuals, 30 c.c. of odour (approximately four times the amounts used in those individuals showing transference) released into the anosmic nostril from the test bottle were not appreciated either in that nostril or in the opposite healthy one. Similarly, sniffing strongly with the *anosmic* nostril did not at any time lead to an appreciation of the odour by the *sound* nostril. Therefore, if any degree of crossing of the odour occurred in the nasal passages under these conditions the quantity was insufficient for the stimulation of the healthy olfactory membrane and the identification of the odour. It may thus be concluded that under the conditions of the experiment much smaller quantities, such as were required for the demonstration of the transference in the twelve recorded cases, would have still less chance of stimulating the opposite healthy olfactory membrane.

(5) In order to determine whether, in normal individuals, any or all of the odour injected into one nostril may cross in the nasal passages to stimulate the opposite olfactory membrane, it was decided to produce a state of unilateral anosmia. This was obtained by spraying the olfactory membrane on one side with 1 per cent. novocain from an atomizer with a long slender tip. It was found that unilateral anosmia could readily be produced and that then blast injections and sniffing of an odour

on that side did not lead to an appreciation of the odour by the other side. Hence, it was concluded that blast injections of the odour did not cross in sufficient quantities in the nasal passages to result in an appreciation of the odour by the normal olfactory membrane.

(6) In olfactory studies by blast and stream injections the normal individual almost always correctly lateralizes the odour or else states that he cannot say on which side it is detected. He never consistently refers it to the opposite side while failing to detect it on the side of injection. The individuals showing transference, however, were never in doubt concerning the side which they thought had been stimulated. They all readily appreciated the stimulus but lateralized it incorrectly. No individual tested knew on which side the odour was injected, as the nosepiece fitted into both nostrils, although only one limb was patent. Repeated examination, suggestion and cross-examination failed to change them in their opinion ; indeed, in several instances, when the nosepiece was demonstrated to them, the odour continued to be appreciated on the wrong side even though the patient realized that the odour was injected into the opposite nostril.

We are thus forced to the conclusion that a condition, which may tentatively be termed olfactory alloæsthesia, exists in these individuals. A stimulus applied to one olfactory membrane is appreciated as if it arose from the other side of the nose. It may be advisable at this point in the discussion to consider briefly what has been described concerning alloæsthesia in general.

*Sensory alloæsthesia.*—Obersteiner (1881) was the first to give a clear description of this phenomenon of transference of a sensory stimulus from one side of the body to the other, which he termed "Allocheiria." He described its occurrence in four cases, two of tabes dorsalis, one of spinal cord injury and one of hysteria. He applied the term to a condition in which "though the sensibility is retained more or less completely, the patient is not clear, or is frequently, is not constantly, in error as to which side of the body has been touched. The stimulus is commonly referred to the corresponding point on the opposite limbs." Since that time numerous instances of alloæsthesia have been reported but little attention has been paid to its significance. It has been observed in hysteria (Obersteiner, 1881, Bosc, 1892, Verrier, 1898, Jones, 1907, &c.), in spinal cord injury (Obersteiner, 1881, Camp, 1908), in diseases of the spinal cord, notably in tabes dorsalis (Obersteiner, 1881, Déjerine, 1914, Hammond, 1883), following a head injury (Ferrier, 1882), in a brain tumour (Schilder, 1935), in hemiplegia (Kramer, 1915, Bosc, 1892), in

bulbar apoplexy (Kramer, 1915), and in diphtheritic paralysis (Gay, 1893). In all the above instances a touch or prick stimulus applied to one side of the body was referred to a corresponding site on the other side ; the transference in each case occurred in only one direction, viz. from the diseased to the healthy side of the body.

Brown-Séquard (1886) and Mott (1893) both observed it following hemisection of the spinal cord in monkeys. Dusser de Barenne produced local hyperexcitability of one side of a spinal cord segment of a dog by the application of strychnine and cut the sensory spinal pathways above the strychninized area on the same side. He then found that a stimulus applied to the other side was felt on the side of strychninization. It thus seems that hyperexcitability and simultaneous interruption of the sensory pathways on one side leads to irradiation of impulses to symmetrical parts.

Schilder (1935) records the case of a woman who, following a left-sided capsular and parietal vascular accident, showed a transfer of sensation from the left (healthy) side to the right (paralysed) side. There are only two other instances of such a transfer (Hammond, 1883, and Brown-Séquard, 1886). In all other cases the sensation was transferred from the diseased to the healthy side, as in nine of our twelve cases. Schilder (1935) has also described a case of brain tumour in which pin-prick on the left side of the body was appreciated on a corresponding point on the right side, although the patient would often scratch himself where he had been pricked. A pin-prick on the right side was localized with approximate accuracy. Pin-pricks on the face were always correctly lateralized. At autopsy a glioma was found to extend throughout the whole ventricular system involving both frontal lobes and the corpus callosum.

*Auditory alloæsthesia.*—There are three records under this title in the literature. The first, that of Gellé (1888) appears to be of doubtful nature. The second and third, published by Bonnier (1904) are described in detail. In both his cases a plug of wax in one meatus caused pain, deafness and unilateral forced movements, &c., which were referred to the opposite ear. Removal of the wax resulted in cessation of symptoms.

*Visual alloæsthesia.*—Two cases are recorded. Féré (1888) under the title of " Optic Allocheiria," described a female hysteric in whom the visual impression received by the right open eye was regularly referred to the left eye, the patient insisting that she received the impression with the left eye, which in fact was closed. Magnin (1888) also recorded a case of " Visual Allocheiria." An hysterical woman had total and complete left hemianæsthesia, which included the conjunctiva, cornea, auditory meatus and mucous membrane of mouth and pharynx. Smell, taste and hearing

were abolished on the left side, and on this side there were also absolute achromatopsia and almost complete amaurosis. During hypnosis when both eyes were open, but their fields separated by a screen, a coloured object held in front of the left eye was recognized and the patient maintained that she saw the colour with the right eye.

*Gustatory alloæsthesia.*—Ferrier (1882) has recorded the case of a man who, following a blow on the head which rendered him unconscious for sixteen hours, developed complete alloæsthesia in both lower limbs and in the mucous membranes of mouth, tongue and nasal passages. Sensibility was intact throughout. A substance placed on one side of the tongue was tasted on the opposite side, although touch sensation itself was also transferred in the same direction. With the eyes bandaged, a touch stimulus was applied to one nostril and found to be regularly referred to the opposite nostril. Ferrier noted that as far as could be judged, the patient's sense of smell not being very acute, it was impossible to determine whether there was reversal of smell proper but only as regards the common sensibility of the nostril. The alloæsthesia persisted for five months.

We have been unable to find any reference to olfactory alloæsthesia in the literature.

### Theory Propounded to Explain Alloæsthesia.

In 1883 Hammond put forward an hypothesis which has been considered an adequate explanation of alloæsthesia by the majority of writers on the subject. Following his study of the condition in a case of lateral sclerosis he concluded that " with a lesion in one posterior horn the sensation would be directed through the grey commissural fibres to the other posterior horn and would reach the cortical centre in the corresponding hemisphere, the sensation being then referred by this hemisphere to the wrong side of the body." Brown-Séquard in accepting this explanation stated that " Je ne crois pas qu'il y ait dans les faits d'allochirie rien de difficile à expliquer aujourd'hui que l'on sait que les deux moietiés de la moelle épinière, comme les deux moietiés de l'encéphale, ont de très nombreuses communications et que chacune de ces moietiés peut remplir le rôle de l'autre. On comprend donc aisément comment les impressions sensitives venues d'un côté du corps peuvent être percues comme si elles provenaient du côté opposé." It is difficult, however, to understand why, if alloæsthesia in spinal cord disease and injury is due to a unilateral lesion, it occurs so rarely. Bosc, in discussing his case of fatal cerebral hæmorrhage showing alloæsthesia, considered that impulses reaching the diseased cerebral hemisphere crossed through the corpus callosum to the opposite

side and so were referred to the corresponding side of the body. This "blocking" hypothesis, whether applied to spinal or cerebral cases of alloæsthesia, received trenchant criticism from Jones (1907) who in turn considered the phenomenon to be an affection of "sidedness," due to psychical disaggregation. To the author, Hammond's theory does at least appear to offer an explanation which can account for the conditions described. A tumour in one cerebral hemisphere may prevent the correct perception and identification of an olfactory stimulus on that side, so that the impulse is in turn diverted to the opposite olfactory centres via the anterior and hippocampal commissures. It would then be referred to the nostril of that side. However, more accurate knowledge of the minute anatomy and the physiology of the rhinencephalon is required before the problem can be solved.

SUMMARY.

(1) A condition has been described which has been tentatively termed olfactory alloæsthesia, in which a stimulus applied to one olfactory membrane is not appreciated on that side but is thought to arise in the opposite nostril.

(2) It is elicited in the majority of cases by first applying a prolonged stimulus to the olfactory membrane of that side, followed by injections at threshold level on the same side.

(3) In nine of the twelve recorded instances a cerebral tumour was found on the side from which the odours were transferred. A transference occurred from the diseased to the healthy side. In the three remaining cases a tumour existed on the opposite side. Transference occurred from the healthy to the diseased side.

(4) A brief discussion of alloæsthesia is presented and a hypothesis considered which may account for the phenomenon.

It is a pleasure to express my gratitude to Dr. Charles A. Elsberg for his encouragement and advice during the course of this investigation.

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# DIFFERENCES BETWEEN EXPERIMENTAL RIGIDITIES IN CATS.

BY E. G. T. LIDDELL.

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An earlier account described the effect of acute decerebration upon limb posture in cats some time after making experimental lesions of the spinal cord (Liddell, 1934, 1936). The lesion of the cord, which was on one side only, was originally and chiefly ventrolateral, but by spread of scar-tissue became also partly dorsolateral. It produced ipsilateral limb rigidity, i.e. hypertonia, presumably by "release" from some undefined control. Subsequent acute decerebration at intercollicular level wrought a remarkable alteration. The rigid limb became flaccid, the previously normal limb became rigid. Closer examination showed that the newly rigid limb was showing the classical decerebrate rigidity of Sherrington (1898), with "clasp-knife" collapse, whereas the now flaccid limb which had been rigid before decerebration, had been steadily resistant all the time that flexion was forced upon it, and there had been no clasp-knife collapse. Here, therefore, were two different types of rigidity producible at different times in the same preparation, and meriting further observation. As these results had not been due to the primary surgical lesion in the ventrolateral region but to the dorsally spreading scar, it was decided to make primary dorsolateral lesions, involving specially corticospinal pathways, and that has been done. Justified criticism is often levelled against spinal lesions in that they injure so much more than is intended and because "compensation" is so readily established. Compensation, however, at least in part, may be merely recovery from post-operative œdema which, in cats, is severe. As for the accurate determination of locality, it is well recognized that, even at best, histological methods can show reliably only dead tissue, as a rule, and not sick tissue which may subsequently recover.

## Methods.

Cats were used to the total of twenty-five, and allowing for the severity of the experimental procedures and the functional instability of preparations rostrally decerebrated, gave consistent results. The level of the cord-lesion was either that of the last rib, or in the lower part of the cervical

region. The lesion was made with a Graefe knife, in the dorsolateral region of the cord (fig. 1), during nembutal anæsthesia and after aseptic exposure of the cord by partial laminectomy for a few millimetres. The lateral edge of the dorsal columns is easily defined and makes a reliable guide to the dorsolateral region. Silk sutures closed the muscle-layers and skin. For the next day or two, during recovery from the anæsthetic and the severest stage of cord œdema, no condition stands out definitely. On the whole, recovery from œdema is quicker, or its results in the lower limb less apparent, when the cord-lesion has been placed in the cervical region. The animal begins to walk freely about the fourth or fifth day, with normal gait. If recovery of walking ability is delayed, there may be noted, as on

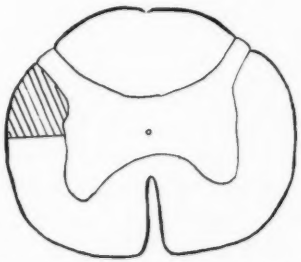

FIG. 1.—Diagram to show approximate extent of lesion in dorsolateral region of cord.

previous occasions, a distended bladded, out of control. Bladder control and ability to walk return together. A simple tension-spring dynamometer with a pan for pressing against the pad of the foot was held in the hand and used to flex the limb and measure the force needed. The flexing force must be imposed at the same rate at each trial, in order to assess accurately the plasticity of each limb.

## RESULTS.

Within two weeks of the operation, such activities as running, jumping and climbing are frequent, without any abnormality in the gait. When, however, the animal is nursed on one's knee, its trunk supported more or less vertically, its limbs protruded and partly hanging, the limb on the side of the cord lesion is evidently extended. (Upper limb changes are not considered here.) As previously mentioned (Liddell, 1936), this method of examination advocated by Langworthy (1928*a*) is essential for unmasking this kind of rigidity in cats, a finding which has since been confirmed by Bard and Rioch (1937). Thus when the cat is at rest, with its attention

gently abstracted, the observer applies hand-pressure to its pad, or grips the ankle in order to flex the limb. Resistance of the muscles in the protruded limb, that is, on the side of the cord-lesion, is at once apparent. The protrusion, therefore, is not due to a paralytic hanging down, but is due to a contraction of those muscles which resist flexion. In an actively protruded limb, moreover, the ankle is usually well extended and not semi-flexed, as in a paralytic limb. With the dynamometer, a flexing force of 2 kg. or more may be registered as necessary for complete flexion, while the limb on the normal side needs only 1 kg. or less of pressure. Such readings are found in cats weighing 2 to 2·5 kg. If the animal is, at first, excited and tense, an increment of 1 kg. or more may be found equally on the two sides, but the difference between each total remains as before. After the first week, with the lessening of œdema in the cord, there may be some small addition, e.g. 0·3 to 0·5 kg. to both sides, but rather more on the normal side, as voluntary power returns fully. This is a more frequent occurrence when the lesion is at thoraco-lumbar rather than cervical level. There may, however, be an actual reduction in readings on the normal side, due, in reality, to a sharp voluntary withdrawal as soon as the pad is touched by the dynamometer pan. Subsidiary reactions in the rigid limb are (i) a flexion reflex from a pinch with a prolonged latent period, but often sharp enough when once elicited; (ii) a diminished ability voluntarily to flex the limb when struggling. The rigidity itself is a solid persisting resistance to the forced flexion, not altered in character but somewhat greater in amount when pressure is applied to the pad than when flexing force is applied to the malleoli by means of a loop of bandage. This slight difference might be expected from our knowledge of the positive Supporting Reaction (Magnus, 1926). The rigidity lasts to the very end of the flexion movement and there is no clasp-knife collapse as in decerebrate rigidity.

### Rostral Decerebration.

That further interruption of the cerebrospinal pathways, other than that already achieved by the dorsolateral lesion, exercises no incremental effect upon the rigidity described, can be shown by acute rostral decerebration, under temporary ether anæsthesia and with temporary occlusion of the carotid arteries. Cortical tissue is completely removed and the central neuraxis is transected about the level of Winkler and Potter's section V (fig. 2). To examine such preparations, the method has to be modified in order to minimize the effects of their characteristic running movements, which, as is well known, begin some thirty to forty minutes after the transection and are generally held to mark the emergence of the preparation

from "shock." The preparation is suspended from a high stand by two ligatures, one from the crown of the head, the other from the rump, so that the claws and feet have no place of purchase. If the preparation is laid on a table, or, if when suspended, the limbs are handled too much, severe spasms of running movements are frequent and the preparation becomes most unstable and inaccessible to examination. Then follow hyperpnœa and cardiac acceleration which lead to an early death from subtentorial hæmorrhage (Girndt, 1926). The risk of hæmorrhage appears at all times to be much reduced also by a diet of milk for some days preceding decerebration, although arterial pressure is raised thereby (Liddell and

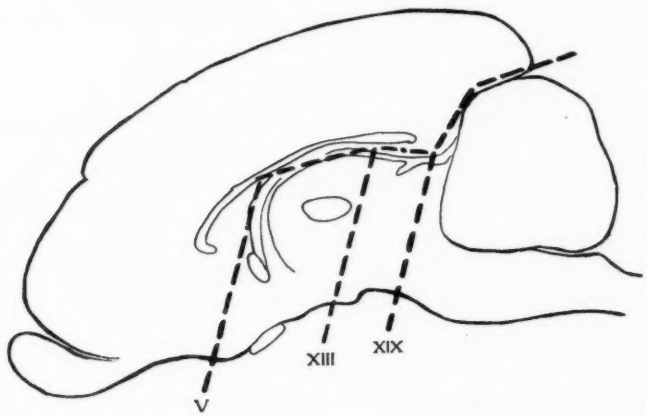


FIG. 2.—Diagram, after Winkler and Potter (1914), to show levels of decerebration. Cortical tissue is removed entirely and the brain-stem then transected at Winkler and Potter's levels. Level V is rostral to the greater part of the globus pallidus and to the crossing of the anterior commissure. Level XIII cuts the corpus callosum proximally from its splenium and, ventrally, is rostral to the corpora mammillaria. Level XIX passes between the anterior and posterior corpora quadrigemina.

Carleton, 1937). Milk, therefore, is now always given to cats for some days before cerebral operations. Black cats, however, do seem specially liable to hæmorrhage.

Thus examined, it is evident within half an hour that the limb which before was the more rigid, is still the more rigid of the two. This may not appear until the carotid arteries, which were looped with loose ligatures before rostral decerebration, are released so as to give rostral tissues a better blood-supply. If the loops are tautened again, the limb differences may subside. This observation, not a constant one, suggests that rostral sub-

cortical tissues play some part in the difference of limb rigidity (see also Liddell, 1938). In short, therefore, the limb rigidity which was previously established by the dorsolateral cord lesion has not been qualitatively altered by removal of rostral nerve tissues.

The preparation may then be subjected to a second and, this time, intercollicular transection of the brain-stem, as described below. Or it may be kept for six hours or more, during which time the neurological state remains unaltered, so long as the heart and respiration continues in activity.

The data from one such case will serve for illustration:—

Dorsolateral lesion of cord, left side, mid-cervical level. Wt. of cat 2·4 kg.

| | | | | |
|---|---|---|---|---|
| (*a*) 4 days later | left hind-limb | 2·2 kg., | right hind-limb | 1·5 k.g. |
| (*b*) 7 „ after (*a*) and 1 hr. after rostral decerebration | „ | 2·3 „ | „ | 1·5 „ |
| (*c*) 1 hr. after intercollicular decerebration | „ | 1·1 „ | „ | 1·1 „ |

### Precollicular Transection.

If, instead of the rostral decereibration described above, the brain-stem is transected more caudally, e.g. Winkler and Potter's level XIII (1914) (fig. 2), there may be the same unaltered state as in rostral decerebrations. Or there may be a change, and the previously rigid limb becomes less rigid and approaches the condition of its fellow, which may be beginning to show some traces of decerebrate rigidity.

Data from such preparations are as follows:—

Dorsolateral lesion of cord, left side, mid-cervical level. Wt. of cat 2·6 kg.

| | | | | |
|---|---|---|---|---|
| (*a*) 12 days later, | left hind-limb | 2·2 kg., | right hind-limb | 1·0 kg. |
| (*b*) 1½ hrs. after precollicular decerebration | „ | 2·4 „ | „ | 1·8 „ |
| (*c*) 1½ hrs. after intercollicular section, and 3½ hrs. after (*b*) | „ | 2·5 „ | „ | 2·5 „ |

Same lesion as above. Wt. of cat 1·9 kg.

| | | | | |
|---|---|---|---|---|
| (*a*) 30 days later, | left hind-limb | 1·5 kg., | right hind-limb | 0·5 kg. |
| (*b*) 1½ hrs. after precollicular decerebration, | „ | 1·1 „ | „ | 1·1 „ |

### Intercollicular Transection.

This is Winkler and Potter's level XIX, for which the carotid arteries are permanently ligated. Whether the preparation is fresh or has been

## ERRATUM.

*Brain*, Vol. 61, 1938. On page 407, line 2; *for* "slightly less flaccid," *read* "slightly less rigid."

previously decerebrated more rostrally, either the limbs become equally rigid or the previously rigid limb may be slightly less flaccid than its fellow, as indicated by the examples quoted. In the latter event, the smaller degree of rigidity on the operated side can be safely ascribed to the observation by Sherrington (1898) that dorsolateral lesions, especially at the thoracic level, may reduce decerebrate rigidity, though not so fully as do ventrolateral lesions. The former result, i.e. equal rigidity, is a common one.

## Discussion.

Experiments to investigate posture modify or impair it in different ways. Hence comes in the cat a solid persisting rigidity in extensors, after cortical lesions or dorsolateral spinal lesions; a "clasp-knife" rigidity with exaggerated postural precedence in extensors, as in decerebrate rigidity, or a co-contraction with diminished but still overpowering precedence for extensors, as in the positive Supporting Reaction. By what nerve-paths or the balance of action of what mechanisms these modifications or reductions of normal posture are brought about, remain still to seek.

These present results accord with the earlier experiments, described in the introduction to this paper. In the present series, the original lesion is dorsolateral and its effect circumscribed by avoidance of secondary effects from scar through a shorter duration of experiment. In any preparation decerebrated at intercollicular level, a ventrolateral lesion is a profound reducer of rigidity. In the undecerebrate animal, such a lesion does not reduce and may even enhance the rigidity from a dorsolateral lesion. Thus it is only when interruptions are both dorso- and ventrolateral that rigidity is severe enough to appear in the cat's gait as spasticity (Liddell, 1936).

The postural over-action released here in the first stage of the experiment by the dorsolateral spinal lesion alone, although almost equal to the body-weight of the animal, is overshadowed in the gait, which, as Graham Brown has emphasized, is basically a spinal rhythm. (Graham Brown, 1914, *a*, *b*.) Only when the animal is quietly nursed on the operator's lap is the rigidity revealed.

Subsequent acute removal, under ether anæsthesia, of cortical tissue ("rostral decerebration"), leaving only basal tissue, does not alter in quality or quantity the pre-existing postural state. But as the decerebrating level becomes more caudal and approaches intercollicular level, the pre-existing solid rigidity tends to be replaced by "clasp-knife" rigidity. On the side ipsilateral to the cord lesion, this is of full or slightly diminished amount, for reasons quoted (Sherrington, 1898). On the other, normal, side there is also decerebrate rigidity, here of full amount. The gradual development

of rigidity of this type as intercollicular level is approached is one of its characteristics (Langworthy, 1928 *b*). That after rostral decerebration, there is no alteration of cord-lesion rigidity may be merely that cortico-spinal paths, already severed by the spinal lesion, are now severed again, at the higher level. Since the experiment is acute, the functional significance of the level cannot be accurately defined, but the functional level is not far below the anatomical level of decerebration (Bazett and Penfield, 1922).

At present, however, the main finding is that in one and the same preparation of cat, two expressions of exaggerated posture can be distinguished. In monkeys, Fulton and his colleagues have shown that decerebrate rigidity is to be distinguished from decorticate rigidity (Fulton, 1938). In the former, the fore-limbs are " thrust backward in rigid extension with pronation," in the latter, they assume " a strongly-flexed hemiplegic posture." Thus according to the status of the animal, different lesions bring to light, by release, different expressions of *functio laesa* in the complex nervous machinery which integrates muscle posture.

SUMMARY.

(1) In cats, dorsolateral lesions of the spinal cord on one side are followed by rigidity in the ipsilateral limb. The rigidity is distinct from decerebrate rigidity. Both kinds of rigidity can be demonstrated at different times in one experimental preparation.

(2) The rigidity from the cord lesions steadily resists forced flexion and has no " clasp-knife " collapse. Although the rigidity may resist a flexing force equal to the animal's body-weight, it is not apparent in the gait.

(3) When the animal is decerebrated at intercollicular level, classical decerebrate rigidity develops in the fellow limb, and has " clasp-knife " collapse. The previously rigid limb, ipsilateral to the cord-lesion, alters the quality of its resistance and may now also show a " clasp-knife " collapse. It may, however, show rather less rigidity because the original dorsolateral lesion may have severed some paths which play a small part in sustaining decerebrate rigidity, when this is made to appear by the intercollicular section.

(4) When the level of decerebration is precollicular or at levels so rostral that the decerebration is rather a " decortication," and when classical decerebrate rigidity cannot be expected to develop, the rigidity obtaining from the spinal lesion is often not altered either qualitatively or quantitatively. The pattern of release, therefore, remains unchanged by these forward decerebrations.

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# OBSERVATIONS ON NERVOUS RELEASE.

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Shock or diaschizis in the nervous system is a well-recognized entity. It is an abeyance or reduction of reflex function at neurone-to-neurone junctions, following the interruption of some large path which normally supplies background excitation to the neurone junctions and keeps the neurones in a state of low activity (Sherrington, 1899, von Monakow, 1914, Liddell, 1934). Similar to the conception of shock as a withdrawal of subliminal excitation, is the withdrawal in "release" of low-grade or subliminal inhibition. It is probable that in release there is destroyed a path which normally inhibits in part or whole some integrated group of neurones, so that, after release, the group shows an aspect of activity which previously it did not show. A familiar example of release is the exaggerated postural activity following intercollicular transection of the brain-stem—"decerebrate rigidity" (Sherrington, 1898). Although release, as a rule, is believed often to need some hours or days to declare itself, decerebrate rigidity appears immediately, unless the anæsthetic is very profound indeed.

Now in shock, as Sherrington (1906) showed for spinal pathways, a second interruption of the excitatory path does not seriously deepen the degree of shock produced by the first interruption. In release, therefore, if it is a comparable phenomenon, the second interruption of an inhibitory path should not, or need not, alter or increase the degree of release from the first interruption.

The experiments now described have for their starting point some observations by Sherrington (1899), which were later pursued by McCouch (1924), and by Fulton and McCouch (1937). Sherrington (1899) wrote: "The cat from which the Rolandic area of the cortex has been removed, so as to ablate the whole of the limb centres, if some weeks later decerebrate rigidity be induced in its limbs, yields the rigidity without perceptible difference between the sides, both right and left." "In the monkey, similarly prepared, a great difference between the limbs on the sides is apparent. The rigidity on the side crossed to the cerebral lesion is very much less than on the homonymous side."

### Rigidity after Cortical Lesions (motor area) and the Effect of Subsequent Decerebration.

*Methods.*—Six cats were used in this series. Under nembutal anæsthesia, and with full asepsis, the cruciate sulcus was exposed frontally, by traversing the frontal sinus. The sinus was swabbed with 1 : 1000 acriflavine and gave no septic trouble. The cortical lesion was made on the lips of the cruciate sulcus, by electro-cautery, about 3 mm. square, in order to minimize subsequent paralysis. Preliminary experiments without the cautery had shown that for obtaining a small release of posture, it was not necessary to follow meticulously the accurate localizations of Langworthy (1928). Subcuticular sutures of silk closed the scalp.

Twenty-four hours later, when the effects of anæsthesia had passed, a release of limb posture was found in the contralateral limb, but was not at all evident in the gait. (Only hind-limbs were examined regularly.) In order to reveal the release of posture, the animal must be nursed on one's knee, as described in the preceding paper. An early sign of release is the absence or lessening of the flexor reflex in the affected limb, or a prolongation of the latent period of the reflex. In general, the animal's condition follows closely that after dorsolateral cord lesions, as described in the previous paper (Liddell, 1938). The affected limb is protruded and more rigid than its fellow. Dynamometer readings were taken, as previously described.

*Results.*—The history of one preparation (Animal No. 1 of Table) may be given in some detail. Its lesion covered the outer extremity of the anterior sigmoid gyrus, area C of Langworthy (1928) (fig. 1). The cerebral lesion was on the left hemisphere.

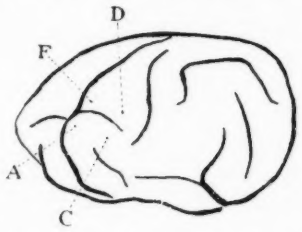


Diagram of cerebral hemisphere of cat, after Langworthy. The lettering of the anterior and posterior sigmoid gyri follows that author.

so that the rigidity developed in the right limbs. The hind-limb showed solidly resistant rigidity, without clasp-knife collapse. After forced flexion, the limb extended again readily, i.e. the flexors were not seriously implicated. The cat weighed 2·2 kg.

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | day | after | cortical | lesion, | left | hind-limb | resistance | 0·2 | kg., | right 1·4 kg. |
| 4 | ,, | ,, | ,, | ,, | | | 0·0 | ,, | ,, | 2·0 ,, |
| 11 | ,, | ,, | ,, | ,, | | | 0·1 | ,, | ,, | 1·5 ,, |
| 20 | ,, | ,, | ,, | ,, | | | 0·4 | ,, | ,, | 2·0 ,, |
| 24 | ,, | ,, | ,, | ,, | | | 0·2 | ,, | ,, | 1·6 ,, |

On the twenty-fourth day, after a rostral decerebration at Winkler and Potter's level V (see fig. 2, previous paper), under ether anæsthesia, the preparation was suspended for examination by strings from the head and rump. The following readings were obtained:—

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 20 | minutes | later, | left | hind-limb | resistance | 1·2 | kg., right hind-limb | 1·2 kg. |
| 30 | ,, | ,, | ,, | | | 1·2 | ,, ,, | 1·4 ,, |
| 40 | ,, | ,, | ,, | | | 0·6 | ,, ,, | 1·4 ,, |
| 50 | ,, | ,, | ,, | | | 0·4 | ,, ,, | 1·0 ,, |
| 60 | ,, | ,, | ,, | | | 0·6 | ,, ,, | 1·2 ,, |
| 135 | ,, | ,, | ,, | | | 1·0 | ,, ,, | 1·5 ,, |

Although these readings fluctuate, the extreme instability of the preparation has to be kept in mind (Girndt, 1926), as well as the gradual passing-off of anæsthesia and "shock." It is evident that the left hind-limb has an accession of postural release from a previous average resistance of 0·8 kg., to a present average resistance of 0·8 kg., while the right limb, previously rigid from the cortical lesion, has suffered some decrease, from 1·7 kg. average to 1·3 kg. average. But the feature to be noted at this stage is that the previously rigid limb is still the more rigid.

150 minutes after transection at level V, the transection was made intercollicular (ether anæsthesia):—

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 10 | minutes | later, | left | hind-limb | resistance | 0·4 | kg., right hind-limb | 1·2 kg. |
| 15 | ,, | ,, | ,, | | | 0·5 | ,, ,, | 1·6 ,, |
| 30 | ,, | ,, | ,, | | | 0·8 | ,, ,, | 1·8 ,, |

Thus, even after intercollicular transection, the previously more rigid limb remains the more rigid. Animal 5, decerebrated at intercollicular level without previous forward decerebration, showed still a difference like animal No. 1, although the cortical lesion had not produced a very marked difference in the otherwise intact animal. Animals 2 and 3 gave trace of previous release after rostral decerebration, though not after intercollicular transection. From these preparations, it is evident that rigidity from decerebration, whether intercollicular or more rostral, need not be by itself a full release, because the release in the previously rigid limb persists and adds itself to the newly established rigidity.

One animal, No. 4, was similarly prepared but was decerebrated at intercollicular level without previous rostral decerebration. It gave results in accordance with those of Sherrington (1899).

Animal 6 shows the difference in resistance between a preparation functionally decerebrated at a low level by looping of the carotids, and the same preparation functionally thalamic, with carotids free. This preparation, so far as the general results of decerebration are concerned, accords with Sherrington's preparations.

## Discussion.

These experiments, though small in number, are significant if related to the results in the previous paper (Liddell, 1938). Here a lesion, established in the motor cortex some three weeks previously, may (but need not) continue to document its release of postural mechanism, even after it has been ablated from the animal, along with all other cortical tissue, in the rostral decerebration. The lesion, though ablated, may assist, and increase the release achieved by acute ablation, which, by itself, is shown in the fellow-limb. In other words, later acute release from decerebration may have added to it the earlier chronic release from the cortical lesion.

## Summary.

The release of postural activity in limb musculature of cats which is wrought by chronic lesions of the motor cortex may remain after the cerebral hemispheres have been removed acutely either by rostral, intermediate or intercollicular decerebration, and the limb which was the more rigid before decerebration, remains the more rigid after it. In continuing its effect, therefore, after acute decerebration, this release shows itself to be a phenomenon with properties comparable to those of its physiological enantiomorph, nervous shock.

TABLE.

| No. of animal | Wt. kg. | Duration of observation period. Days | Lesion | Average limb readings in kg. | | Readings after rostral decerebration | | Time after rostral decerebration | Readings after intercollicular decerebration | | Time after intercollicular decerebration |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | L. hind limb | R. hind limb | Left | Right | | Left | Right | |
| 1 | 2·2 | 24 | Area C (fig. 1) Left side | 0·18 | 1·7 | 0·6 | 1·2 | 1 hr. | 0·8 | 1·8 | ½ hr. |
| 2 | 2·5 | 54 | C + D Left | 0·15 | 1·8 | 1·2 | 2·0 | 1 „ | 0·4 | 0·4 | ½ „ |
| 3 | 2·6 | 55 | D Right | 1·6 | 1·0 | 2·0 | 0·73 | 2 „ | 1·0 | 1·0 | 1½ „ |
| 4 | 2·3 | 23 | C Right | 1·5 | 0·4 | — | — | — | 0·7 | 0·7 | 1 „ |
| 5 | 3·0 | 22 | F Left | 0·8 | 1·1 | — | — | — | 1·3 | 1·8 | 3 hrs. |
| 6 | 2·5 | 27 | A Right | 1·5 | 0·2 | 1·0<br>0·7 | 1·2<br>0·7 | Carotids free<br>Carotids looped | | | |

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# A DEFORMITY OF THE HIND-BRAIN ASSOCIATED WITH INTERNAL HYDROCEPHALUS. ITS RELATION TO THE ARNOLD-CHIARI MALFORMATION.[1]

BY ADAMS A. McCONNELL AND H. LEE PARKER.

On five occasions suboccipital exploration for cerebellar tumour has revealed, instead of a tumour, a deformity of the lower part of the medulla oblongata and a prolongation of the cerebellar tonsils into the spinal canal. The appearance of the parts exposed by operation, and in three of the cases studied post mortem, suggests a relationship to the Arnold-Chiari malformation described in cases of spina bifida.

*Case 1.—Male, aged 18. Headache, vomiting, failing vision. Papill-œdema. Involvement of 11th cranial nerve on left side and of 9th and 12th on the right. Suboccipital exploration, pressure cone and tumour of medulla. Post-mortem examination, deformity of medulla.*

H. C. was admitted to the Richmond Hospital, Dublin, on May 15, 1935, on account of headache and vomiting.

Five months before admission, he began to suffer from attacks of throbbing pain in the frontal and occipital regions and in the back of the neck. These attacks increased steadily in number and severity and later were accompanied by vomiting.

On May 14 paroxysmal headache and incessant vomiting reduced the patient to a stuporous condition, in which condition he arrived in hospital.

*Examination.*—The patient was a sturdy, well-built youth. He was drowsy, stupid and non-coöperative. Temperature 102° F., pulse 100. There were clinical signs of consolidation of the lower lobe of the left lung. Radiological examination confirmed the clinical signs and also revealed slight but typical lesions of early tuberculosis. Papillœdema of 5 D was present in each eye with numerous retinal hæmorrhages and exudate. The right pupil reacted very sluggishly to light; the left was practically inactive. Hearing seemed to be diminished on the right side. There was definite weakness of the right side of the soft palate and weakness and atrophy of the right side of the tongue. On the left side of the body the trapezius muscle was very weak. All tendon reflexes were increased but the plantar responses were flexor.

The pneumonic process cleared up completely in ten days but by this time the papillœdema had increased to 7 D in the right eye and 6 D in the left. There was

[1] An extension of a paper read at the Annual Meeting of the American Neurological Association, Atlantic City, N.J., June, 1937.

marked ataxia in the upper and lower extremities on the left side. The right side was normal. At no time was he able to get up and walk.

Radiological examination of his skull showed digitations all over the vault and some rarefaction of the dorsum sellæ.

A diagnosis was made of tumour in the region of the foramen magnum because of evidence of damage to the lower cranial nerves on both sides and because of the increase of intracranial pressure.

May 30, 1935.—Operation: Avertin and local anæsthesia. The usual exposure of the cerebellum was made. There was a considerable amount of tension in the posterior fossa which was somewhat relieved by tapping a lateral ventricle. The arches of the first and second vertebræ were removed before the dura was opened.

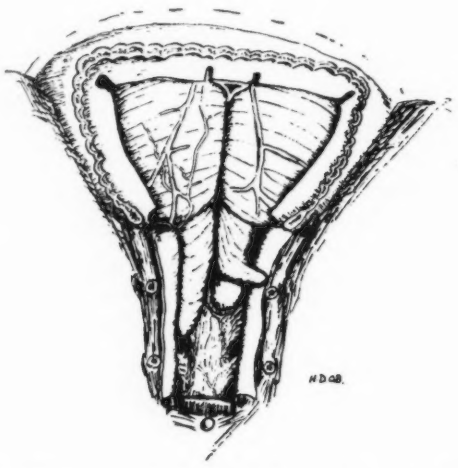

FIG. 1 (*Case 1*).—Diagrammatic sketch of the cerebello-medullary region at the time of operation. The prolongation of the cerebellar tissue below the foramen magnum, the upward course of the cervical nerve roots, and the nodule on the medulla can be seen.

The cerebellar hemispheres bulged through the opening in the dura and a very tense and unusually long pressure cone was present. Separation of the tonsils below the foramen magnum was accompanied by a free flow of cerebrospinal fluid and the tension subsided completely. Further separation disclosed the lower third of the 4th ventricle. When the right side of the pressure cone was displaced, a protuberance was noted on the dorsum of the medulla. It occupied the right half of the closed part of the medulla, and was situated caudal to the foramen magnum. It seemed to rise sharply from the dorsal surface of the cord and to merge gradually into the medulla. The first cervical nerves arose below the level of this nodule and inclined obliquely upwards to their exit from the canal (fig. 1).

The diagnosis at the time was tumour of the medulla oblongata and since a free communication had been established between the 4th ventricle and the subarachnoid space, the operation was concluded.

The patient recovered consciousness shortly after the operation and seemed to be doing well for the next forty-eight hours. He then became suddenly comatose. Ventricular puncture was done immediately. There was no tension in the ventricle and death occurred soon afterwards.

Permission was given for partial necropsy only. The brain was removed entire, but the spinal cord was cut at its junction with the medulla. There was a definite internal hydrocephalus which affected all the ventricles.

Macroscopic examination of the brain and the meninges revealed no other pathological changes. Sections of the brain-stem showed no tumour either grossly or in serial sections examined under the microscope.

*Case 2.—Male, aged 10. Headache, hiccough, staggering gait. No papillœdema. Internal hydrocephalus. Operation, deformity of cerebellum and medulla. Post-mortem examination.*

Q. L. was admitted to the Richmond Hospital, Dublin, on March 29, 1936. His chief complaints were headache and a staggering gait.

Twelve months before admission he had had a very severe attack of bronchopneumonia which lasted for some weeks. He was delirious part of the time. During his convalescence headaches began. They were chiefly situated in the occipital region, more frequently present in the morning upon awakening, and they lasted for a few hours. Vomiting was not common but there were very frequent attacks of hiccough. The staggering gait was noticed soon after the onset of the headaches and both symptoms were becoming increasingly severe.

The child was well-nourished, was confined to bed, and had a marked squint due to paralysis of the left external rectus muscle. The fundi were normal. There was marked nystagmus on lateral gaze, which was present also on looking upward, though to a less degree. His head was normal in size and shape. His speech was scanning in character and there was definite inco-ordination in the upper extremities on performing the usual tests. His tendon reflexes were all exaggerated and the plantar responses were both extensor. The gait was spastic and ataxic, but the patient could make progress unaided.

The differential diagnosis seemed to lie between an arachnoiditis of the cisterna magna secondary to bronchopneumonia and a medulloblastoma of the vermis cerebelli.

On April 2, 1936, the lateral ventricles were tapped and found to be dilated. Thorotrast was injected and rœntgen studies were made. Every portion of the ventricular system was visualized and found to be evenly dilated. No thorotrast, however, had passed into the cisterna magna.

The usual cerebellar exposure was made. The dura was under considerable tension which was relieved at once by puncture of the posterior horn of the lateral ventricle. When the dura mater was opened widely it was found that the cisterna magna was of moderate size and that there was no thickening or opacity of the arachnoid membrane. Both cerebellar hemispheres appeared normal except for the presence of a pressure cone. In order to expose the cone completely the posterior arches of the atlas and axis were removed. On the right side the cone extended downwards to the level of the axis, and on the left side to the upper edge of the lamina of the 3rd cervical vertebra. Each side of the cone was thin and flat with hard and ivory-white tips quite different in appearance from the usual pressure

cone. When the cone was displaced a nodule was seen on the dorsum of the medulla (fig. 2). Further separation opened the 4th ventricle and there was a free flow of fluid mixed with thorotrast.

The calamus scriptorius was at the level of the foramen magnum. The nodule appeared to be on the right side of the closed part of the medulla and below the foramen magnum. The lower part bulged sharply backwards from the brain stem but its upper part faded away gradually. It was about half a centimetre long and a little less than that in width and just barely crossed the middle line. The first and second cervical nerves emerged from the cord below the nodule and inclined upwards. The wound was closed in the usual way. The patient's general condition was good at the end of the operation, but later there was some cyanosis although the breathing was not markedly embarrassed. Death occurred suddenly at 10 p.m. that night.

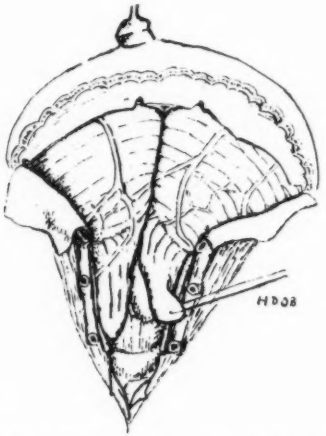

FIG. 2 (*Case* 2).—Sketch showing prolongation of the cerebellum into the spinal canal. The hardened tips of the cerebellar tissue have been separated diagrammatically to show the nodule on the dorsum of the medulla.

Necropsy was performed on the day of death, and as in Case 1 was limited to an examination of the brain and upper portion of the spinal cord. The operative findings were confirmed. Sections of the whole brain and of the brain stem in particular failed to disclose any neoplastic or other cause for the symptoms other than the deformity of medulla and cerebellum.

*Case 3.—Female, aged 32. Buzzing noise in head, vomiting. Later headache and staggering gait. Late onset of slight papillœdema. Marked internal hydrocephalus without tension. Operation, deformity of cerebellum and nodule on medulla. Recovery.*

T. L. was admitted to the Richmond Hospital, Dublin, on February 10, 1936. Her chief complaints were a buzzing noise in her head and vomiting.

In June, 1935, when on holiday, she suddenly became conscious of a buzzing noise in her head.

A month later she began to vomit, chiefly in the morning and without nausea. At first the vomiting occurred about twice a week but later became a daily affair. In August, 1935, headache accompanied the vomiting. The headache was occipito-cervical in location and as time went on became increasingly severe. In December, 1935, she became very unsteady on her feet. Flexion of the head on the chest seemed to relieve the staggering.

At the beginning of her stay in hospital, the outstanding feature was the early morning vomiting. Later on, the headaches became a more prominent feature. The buzzing noise continued without intermission. The eye grounds on repeated examination were normal up to May 10, 1936, when very slight papillœdema appeared. Radiological examination of her skull showed nothing abnormal. Her blood-pressure was 100 millimetres systolic and 60 diastolic.

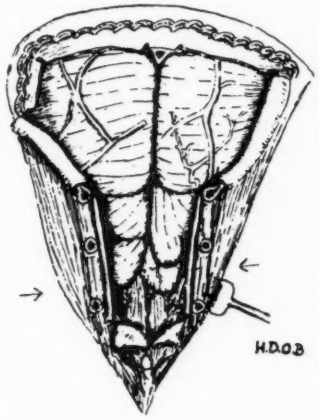


FIG. 3 (*Case 3*).—Diagrammatic sketch of conditions found on removal of the occipital bone atlas and axis.

The first impression of her case was that she was suffering from Addison's disease. Blood urea 20 mg. per cent. Blood sugar 115 mg. per cent. Plasma chloride 592 mg. per cent. Serum calcium 10·1 mg. per cent. B.M.R. – 10.

Frequent neurological examinations showed nothing more than an ataxia of gait commensurate with her profound weakness and her bed-ridden state. On walking she held her head stiffly and tilted to the left. There was no nystagmus.

May 18, 1936.—Ventriculography: When the needle was passed into the ventricle no fluid escaped through it, but 90 c.cm. of fluid were gradually aspirated and replaced by air. The pictures showed a marked internal hydrocephalus involving the 3rd and 4th ventricles. The diagnosis of adhesions obstructing the outflow of cerebrospinal fluid from the 4th ventricle was made. The cerebrospinal fluid was normal in every respect.

Immediately after the ventriculography the posterior fossa was explored in the usual manner under local anæsthesia. There was no tension when the dura was

exposed, and on opening it, bubbles of air were seen in the cisterna magna. The cerebellar hemispheres appeared normal, except for a very marked prolongation of the tonsils which simulated a pressure cone. The right tonsil reached a point below the arch of the atlas, whilst the left extended to that of the axis. The right tonsil was rather bulky as was the upper part of the left, but the lower third of the latter was thin, feathery and rather yellow. Appearing under the right tonsil was a whitish nodule rising abruptly from the brain-stem and occupying apparently all the right side of the medulla (fig. 3). Its widest part was below the level of the arch of the atlas. The first cervical nerve emerged from the cord just below the nodule and ascended obliquely upwards to its exit from the spinal canal. There seemed to be abundance of room for the structures passing through the foramen magnum. The presence of air bubbles in the cisterna magna indicated that there was no obstruction to the exit of cerebrospinal fluid from the 4th ventricle. Accordingly nothing more was done and the wound was closed.

The patient had a slow convalescence. At intervals of four or five days she complained of severe frontal headaches associated with vomiting. These attacks were always relieved by the withdrawal of 10 c.cm. of fluid from a lateral ventricle, but it is interesting to note that the fluid was never under tension and had to be aspirated. Similar relief was obtained later during her convalescence by the administration of magnesium sulphate by mouth. She returned to her work as a waitress in September, 1936.

For the next seven months she frequently wakened in the morning with a feeling of nausea which continued until she "retched" up with difficulty about a teaspoonful of yellow or green fluid.

The patient was last seen in June, 1938, more than two years after the operation. She was cheerful, comfortably fat and "able for anything." She stated that she occasionally "brought up a mouthful of bitter stuff" in the morning and that she was quite unable to eat anything until the afternoon. The cerebellar decompression was flat. There was no trace of staggering in her gait and no abnormal neurological signs were found.

*Comment.*—The chief differences between this case and the two preceding were the more insidious onset, the relatively few signs of involvement of the central nervous system, and the successful outcome. The surgical findings were essentially the same and the appearance at operation suggested that the prolongation of the cerebellar tonsils into the spinal canal had been present for a considerable period and was not a recent occurrence. A similar nodule or knuckle was present on the dorsum of the medulla. It is noteworthy that there were no signs of increased intracranial pressure either on examination of the eye grounds, at the operation, or on tapping the ventricles after operation. The cause of the patient's symptoms must remain unexplained. The result was excellent and it is possible that her recovery was due to the fact that no attempt was made to liberate the cerebellar tonsils.

*Case 4.—Female, aged 26. Headache and failing vision. Papillœdema. Pulmonary tuberculosis. Cerebellar exploration, deformity of medulla. Recovery.*

B. J. was admitted to the Richmond Hospital, Dublin, on March 4, 1938, on account of headache and failing vision.

One month before admission she noticed that she had some difficulty in reading the paper and in sewing. About the same time she began to wake about 7.30 a.m. with a slight headache which grew worse until she had dinner at 1 p.m. when it gradually subsided but never completely disappeared. "Headache powders" often

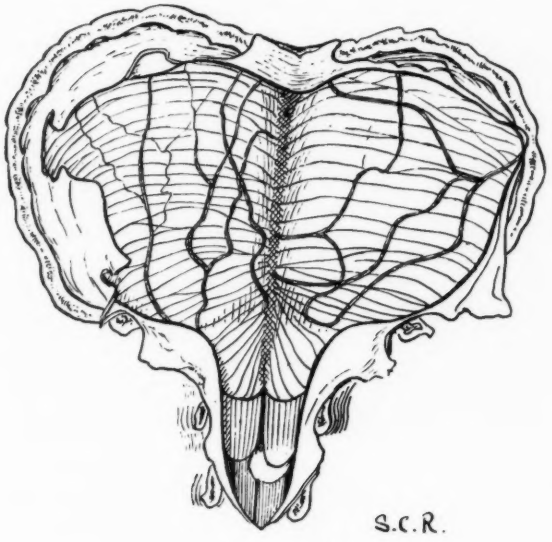


FIG. 4.

gave partial relief. The headache was always frontal in position and dull in character. Occasionally the patient felt dizzy but she never staggered nor fell. Family history good.

*Examination.*—The patient was thin, mentally alert and co-operative. Weight was 8 st. 7 lb. Apart from bilateral papillœdema of 5 D and slight weakness of the left external rectus muscle the cranial nerves were normal. There was slight tremor in both hands and some uncertainty in carrying out the finger-nose test. The knee-jerks were slightly exaggerated and the right plantar response was extensor. The gait was normal. The blood-pressure was 110 systolic, 75 diastolic. Clinical examination of the chest revealed nothing abnormal, but radiography showed numerous discrete opacities which were regarded as typical of miliary tuberculosis.

The diagnosis of tuberculoma of the cerebellum was made, and a cerebellar decompression advised.

March 7.—Ventriculography showed definite internal hydrocephalus involving the 3rd ventricle. The 4th ventricle was not visible.

Under local anæsthesia the usual cerebellar exposure was made and the arch of the atlas removed. There was gross tension. The dura was opened down to the second cervical vertebra. The cerebellar hemispheres were symmetrical. At this stage the appearance of the structures passing through the foramen magnum suggested a tapering bamboo cane with three short segments each of about 1 cm., the thickest segment being the highest. When the arachnoid was opened the upper segment contained the base of a pressure cone which extended down to just above the level of the atlas. The second segment held the continuation of the pressure cone which was thinner and appeared to be marked off from the proximal part, and the third segment corresponded to a lump on the back of the medulla. The tip of the right tonsil was white and firm though thick, while that on the left side was thinner. The tonsils were freed by the division of the arachnoid round them but because of our experiences with other similar cases we did not separate them to look at the ventricle and we did not inspect the upper spinal nerves. Because of the X-ray appearance of the lungs no exploration was made of the cerebellum itself as we thought there would probably be a tuberculoma. A wide decompression was left.

Fig. 4 is an attempt to represent semi-diagrammatically the appearance of the exposed parts.

The patient's temperature reached 99·8° F. each evening for three days after the operation. She was allowed to get up on the tenth day. That evening her temperature rose to 100, and showed a similar rise each evening for five days, when it became steady. Apart from the temperature she made an excellent recovery and left hospital on March 30.

Subsequent reports indicate that she continues to be free from neurological symptoms. Pulmonary symptoms never developed.

The occurrence of these four cases inside three years suggested that similar cases might have been overlooked. We therefore made a search through the pathological museum and discovered a specimen which had not been recognized five years previously.

*Case 5.—Male, aged 15. Vomiting, headache, defective vision. Papillœdema. Cerebellar exploration. Autopsy, deformity of medulla.*

C. P. was admitted to the Richmond Hospital, Dublin, on August 16, 1933, on account of headache and defective vision.

For two years before admission the patient had attacks of vomiting every two or three weeks. About one month before, he began to suffer from headaches which started in the frontal region and spread to the left occipital region. The headaches lasted for a few minutes and recurred every two or three days. Vision began to fail about a fortnight before his arrival in hospital.

In hospital severe headache and repeated vomiting occurred nearly every morning.

*Examination.*—The boy was well-built. There was papillœdema of 5 D in the

right eye and 6 D in the left. Visual acuity was $\frac{6}{9}$ in each eye and the visual fields were full. The pupils were equal and active. The left external rectus muscle was weak and there was occasional diplopia. Horizontal nystagmus was present and was more marked on looking to the right.

The rest of the neurological examination was negative.

Radiographic examination of the skull showed convolutional atrophy, slight separation of the sutures and some rarefaction of the dorsum sellæ.

August 24.—Ventriculography: There was a gross hydrocephalus involving the lateral and 3rd ventricles. No air was seen in the 4th ventricle. Operation: Cerebellar exposure. There was no fluid in the cisterna magna. The hemispheres were symmetrical and a small area of the vermis appeared between them. The arch of the atlas was removed. A thick pressure cone reached to a point below this

FIG. 5.

level, the left side of the cone being larger than the right. Rather dense adhesions obscured the tip of the left side of the cone and glued the two sides together. When these adhesions were separated there was a free flow of fluid and all tension disappeared. An incision was made into the vermis but no tumour was seen. The impression was that an adhesive arachnoiditis had blocked the passage of fluid from the 4th ventricle and that the pathway had been cleared. The wound was closed. The patient appeared to make a good recovery from the operation and regained full consciousness. About 10.30 that night he was talking cheerfully to the nurse and asked for a drink. At this time the pulse dropped to 60 and the respirations to 10 but inside half an hour they rose to 90 and 20 respectively. The nurse turned away for about one minute and when she turned back the boy was dead, without warning of any sort.

Post-mortem examination.—When the pressure cone was elevated the dorsal aspect of the medulla was seen to be heaped up as a lump, and between it and the spinal cord lay a deep groove. There was no corresponding kink on the anterior aspect of the medulla or cord. The medulla seemed to have undergone a certain amount of torsion around its long axis.

The right half of the pressure cone was removed at the level of the foramen magnum. This revealed that the whole closed part of the medulla had lain in the spinal canal (fig. 5).

When the lower part of the cerebellum was dissected off the roof of the 4th ventricle no foramen of Magendie nor foramina of Luschka could be demonstrated. Fig. 6 shows the intact inferior medullary velum from the right side. The 4th ventricle was greatly distended and the aqueduct of Sylvius dilated, as were the 3rd and lateral ventricles. There was no evidence of a tumour anywhere.

Serial sections showed that the lowest part of the 4th ventricle formed a diverticulum overhanging the dorsal aspect of the central canal of the medulla.

The ependyma of the central canal at this level showed proliferation and lower down the canal was completely obliterated by a loose mass of ependymal cells.

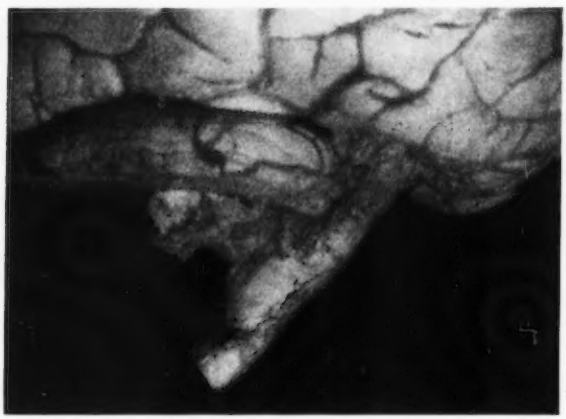

FIG. 6.

## ANATOMY.

The anatomical findings in all these cases were very much alike; each had what appeared to be a pressure cone, in each the closed part of the medulla lay in the spinal canal, in each there was a protuberance on the dorsal aspect of the medulla, and in three some obliquity of the upper cervical nerves was noted. All had internal hydrocephalus involving the 4th ventricle. In all cases the protuberance seemed to be chiefly on the right side of the medulla, and in the post-mortem specimens this appeared to be due to the medulla having undergone a slight amount of axial torsion, its lower part being rotated in a clockwise direction. Fig. 7 shows the consequent asymmetry when viewed from in front.

For convenience in description we have used the term "tonsils" to designate the prolapsed cerebellar tissue.

Spina bifida was not demonstrated in any of the cases, but the spine was not X-rayed in cases 1, 2 and 5. In the second case, however, it was examined after death. In Cases 3 and 4 X-ray examination of the spine was negative. Microscopic examination of the medulla (Cases 1, 2 and 5) revealed a certain amount of distortion, as would be expected, but there were no signs of degeneration or demyelinization. In Case 5 proliferation of the ependyma of the central canal of the medulla was present. Cerebellar histology was normal. A search for "torpedo" bodies was carried out by the method recommended by Aring (1938), but none could be found

FIG. 7 (*Case 5*).—Anterior view showing the asymmetry and the deep grooves formed by the vertebral arteries.

although the axons of the Purkinje cells had apparently been fully stained.

A clue to the significance of the anatomical findings was furnished by a paper by Russell and Donald (1935). These authors reported ten cases of meningomyelocele associated with a malformation of the hind-brain.

"In this a tongue of variable length, consisting of cerebellar tissue and the greatly elongated medulla oblongata, protrudes downwards into the spinal canal. It overlaps and compresses the upper segments of the cervical cord, distending the dural theca in this neighbourhood and filling the

foramen magnum. The cavity of the 4th ventricle extends caudally into this tongue, lying between the cerebellar and medullary components."

"The spinal cord appears abnormally small and the cervical roots always run in a cephalic direction to reach their exits through the dura mater."

"There is a conspicuous hypoplasia of the cerebellum which is usually composed of a small compact mass lacking differentiation into vermis and lateral lobes. The tonsils and flocculi can seldom be identified."

They pointed out that this malformation had been noticed first by Arnold in 1894 and more fully described by Chiari in 1895. Later authors had adopted the name of the Arnold-Chiari malformation.

In one case of meningocele Russell and Donald found that there was caudal displacement of the medulla but that there was no tongue of medullary tissue overlapping the spinal cord as in the fully developed malformation.

We examined six infants with meningomyelocele who had died at or soon after birth. In four of them the fully-fledged Arnold-Chiari malformation was present, but in two the deformity, when exposed as by operation, resembled closely that described in our cases.

The following case came to operation.

Male infant, aged 4 months. Large meningomyelocele. Unsuccessful attempt to close lumbar defect. Cerebellar exposure. Arnold-Chiari malformation. Death.

The infant was healthy and well-nourished. The head was small and the coronal fontanelle just perceptible. There was free movement of both legs. A large meningomyelocele occupied the lumbar region; it measured about three inches in diameter. The skin over it was tense and purple and there had been some leakage of fluid for two days before admission.

July 1, 1938.—Operation: When the sac was opened the lower part of the spinal cord and the cauda equina were found adherent to its dorsal wall. These structures were dissected free without difficulty and the sac itself was reformed. Fascial flaps were reflected and sutured across the defect and a satisfactory closure of the cutaneous wound was made. By the eighth day enough fluid had escaped beneath the skin to float the wound and it was necessary to aspirate the fluid to prevent undue tension. On the twenty-first day the wound seemed to be perfectly healed and aspiration was stopped, but next day it began to leak. During this time the child had been very well and there had been no sign of raised intracranial pressure.

It was decided to expose the region of the brain-stem in the hope of promoting the return flow of fluid from the spinal subarachnoid space. This was done on July 27 through a longitudinal incision. The foramen magnum was very large and between its dorsal lip and the arch of the atlas there was an interval of about one inch through which the cerebellum protruded. There was no vermis. The arches of the atlas and axis were removed and the opening in the dura continued downwards. Coming from the lower part of the cerebellum was a cone-shaped process of arachnoid which was densely adherent to the prolapsed cerebellar tonsils. These extended downwards to the level of the lamina of the 3rd cervical vertebra. The spinal subarachnoid space was opened at this level and there was a free flow of fluid.

The arachnoid membrane was stripped easily from the lower part of the cerebellar hemispheres, but there was no cisterna magna.

In order to give the cerebellum more room, the back of the foramen magnum was removed for about 1 cm.: this exposed the lateral sinus. The dural incision was extended upwards and to the left. The upper surface of the cerebellum was now exposed and there was a space between it and the tentorium. At this stage there was a sharp hæmorrhage, probably from a cerebellar vein joining the deep aspect of the lateral sinus. This was promptly controlled but it must have been a factor in the child's death soon after the operation.

Post-mortem examination was limited to the region of the operation. The cerebellar tonsils and the medulla at that level were completely surrounded by a deep ring of adherent arachnoid membrane. It was impossible to strip off the arachnoid without tearing the underlying structures. The tonsils in their turn were closely adherent to the back of the medulla except in the middle line where there

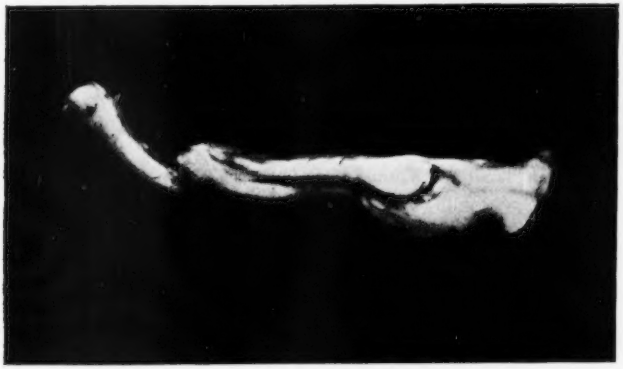

FIG. 8.

was a tiny smooth tunnel passing from the 4th ventricle. It seemed as if the tonsils and closed part of the medulla plugged the upper end of the spinal subarachnoid space as the stopper plugs the neck of a bottle. The minute tunnel might be compared to a perforation through the stopper. Simple opening of the dura would have had no effect on the essential lesion.

These anatomical observations, although unsupported by preoperative tests, tend to confirm the conclusion reached by Russell and Donald that the cerebrospinal fluid can get into the spinal subarachnoid space but cannot get out of it.

The usual protuberance was present on the dorsal aspect of the medulla and there was a corresponding kink on the anterior aspect of the brain stem (fig. 8).

The 4th ventricle was large but not distended, and the aqueduct of Sylvius was small and patent. The upper cervical nerves were oblique.

The operative findings in this undoubted example of the Arnold-Chiari malformation resembled in part those of Case 5. In both the cerebellar cone just covered the closed part of the medulla and concealed the protuberance on the latter: in both the arachnoid membrane was adherent to the cone.

In the true Arnold-Chiari malformation with spina bifida there are

many degrees and the lesser degrees recall the conditions found in our five cases. In these cases, however, the unstrippable adhesions, which were constant in the infants, were never found. Until the whole spinal canal can be opened up and the spinal cord examined in some similar case it is impossible to express an opinion on the real relationship of these cases to those of the Arnold-Chiari malformation.

### Clinical Features.

The chief symptoms and signs of our cases are presented in the following table:—

| Case | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Age | 18 | 10 | 32 | 26 | 15 |
| Headache | + | + | + | + | + |
| Vomiting | + | − | + | − | + |
| Papilloedema | + | − | − | + | + |
| Ataxia | left side | ++ | ++ | arms | − |
| Exaggerated reflexes | + | + | − | + | − |
| Babinski | − | + | − | R. | − |
| Nystagmus | − | ++ | − | − | + |
| Cranial nerve weakness | R. 9 and 12 L. 11 | L. 6 | − | L. 6 | L. 6 |

There was no uniform symptomatology in these cases, and nothing that would suggest the presence of this condition in a new case. On one occasion we made a tentative preoperative diagnosis, but syringobulbia was demonstrated later.

In general, except in Case 1, the clinical aspect of these cases was that of obstructive internal hydrocephalus without localizing signs.

Ventriculography was disappointing: although the 4th ventricle was grossly dilated in all the cases, it was visible in two only.

### Surgical Considerations.

*Recognition.*—It may not be easy to recognize this condition at operation if the cerebellar tonsils are thick and completely cover the medulla, as in Case 5. Suspicion should be aroused if the arachnoid is adherent to the tonsils or if the tonsils themselves appear flatter than they usually are in a pressure cone, or if they are feathery or white.

If the protuberance on the dorsal surface of the medulla is seen, the suspicion is confirmed, but if it is not, obliquity of the upper cervical nerves should be looked for. Of course the presence or history of spina bifida would be significant.

*Problem of treatment.*—In the first two cases the arachnoid membrane was widely opened from the cisterna magna to the spinal subarachnoid

space. It was not adherent to the tonsils. The latter were separated from each other and lifted from the medulla in order to open up the 4th ventricle. This manipulation was easy, and the separation bloodless, and at the end of the operation the tonsils lay loosely where they had lain at the beginning. Both patients died: one in forty-eight hours, the other in eight. Microscopic examination did not reveal any cause for the fatalities.

In the next two cases, when the arachnoid was widely opened as before and the condition recognized, nothing more was done. Both patients survive and are well.

Case 5 differed from the others in two respects. First, the arachnoid was adherent to the tonsils; and second, the 4th ventricle was closed. The arachnoid was dissected off the tonsils and the latter were mobilized. Neglect to open the 4th ventricle was a serious error. The patient died in ten hours. In the infant with the meningomyelocele the spinal cord was freed from its attachment to the sac at the first operation and later the subarachnoid space was opened widely above and below the band of adherent arachnoid which encircled the cerebellar cone and the medulla. The cone was not touched. We think that this infant died because of hæmorrhage during the operation.

In the light of these results, it would seem that the safest thing to do is to open the arachnoid widely from the region of the cisterna magna to the spinal subarachnoid space and to do nothing more. If the arachnoid is adherent to the tonsils, it should be left adherent, and the subarachnoid space opened above and below. The tonsils should not be mobilized.

If there is no outlet from the 4th ventricle as in Case 5, and if mobilization of the cerebellar tonsils is as dangerous as we think it is, it would seem necessary to split the vermis, or to short circuit the cerebrospinal fluid by opening the 3rd ventricle.

These therapeutic speculations apply only to the degrees of the malformation that we have described, for there are probably many other degrees which we have not met with and which may present different surgical problems.

SUMMARY.

A deformity of the brain stem and cerebellum in children and adults is described. It is suggested that this deformity is a minor degree of the Arnold-Chiari malformation found in association with meningomyelocele.

Tentative suggestions for treatment are advanced.

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# FAMILIAL NEUROMYELITIS OPTICA: ITS OCCURRENCE IN IDENTICAL TWINS.

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THE condition known as neuromyelitis optica is still of sufficient rarity to merit attention, not only on clinical and pathological grounds, but also because its relationship to other members of the demyelinating group of diseases remains uncertain. No example of familial neuromyelitis optica has been reported in the literature. This paper contains an account of this disease, as it occurred in identical twins.

Alice K. and Dorothy K. were born on September 8th, 1909; there was one placenta. When four months old they both suffered from bronchitis, at six years from measles, and at eighteen years from chickenpox. The onset of menstruation occurred at the same time in both. In their facial appearance, colouring, body configuration, temperament, scholastic and games ability they were alike.

The following is an account of the illness which proved fatal to them both.

*Case 1.—Female, aged 24. Following "influenza" developed an acute dorsal myelitis; subsequent improvement. Five months after onset blindness and recurrence of dorsal myelitis with spread to cervical cord. No return of vision. Bed sores and a bladder infection led to death eighteen months after onset.*

Alice K., aged 24, on January 16, 1933, developed a cough without sore throat which was thought to be "influenza". On January 20 she experienced severe pain across the shoulders which persisted for several days. On January 26 she noticed tingling in the left thigh followed by numbness which spread upwards to the abdomen and then affected the right leg in the course of three days. On January 27 the legs became weak and she had retention of urine which lasted for two days. On January 30 she was admitted to the Neurological Ward of the Middlesex Hospital. The temperature was normal. She was an intelligent patient. The cranial nerves and upper limbs were normal. There was paresis of the lower intercostal and abdominal muscles and of the lower limbs, the right leg being more affected than the left. The abdominal reflexes were absent; the left knee-jerk was slightly increased, whilst the right was diminished. Both ankle-jerks were brisk. The plantar responses were extensor;

a flexion withdrawal reflex could easily be elicited. All forms of sensation were diminished on the trunk below the 4th dorsal segment. Tactile sensation was unimpaired on both legs ; thermal and pin-prick sensation were retained below the 3rd lumbar segment on the right side, but were absent on the left leg. Vibration sense was absent, but postural sense was normal. There was retention of urine and incontinence of fæces. A lumbar puncture showed a clear fluid ; the Wassermann reaction was negative, 4 lymphocytes per c.mm., protein 0·03 per cent., Lange colloidal gold curve 1111222100. On February 3 the paraplegia was more marked. Both knee-jerks were now absent, whilst the ankle-jerks remained brisk. Thermal and pin-prick sensation were now lost in the right leg, but postural sense remained unaffected. During the course of the next three days the paralysis in the lower limbs became almost complete. However, by the end of February, power had improved in the left leg, and the knee-jerks were feebly present. Thermal and pin-prick sensation returned in the right leg and later in the left leg. Vibration sense remained impaired up to the beginning of April, whilst postural sense was retained, except on two consecutive days. Sphincter control returned, and the patient was discharged on May 4 with a moderately severe spastic paraplegia which, however, did not prevent her from walking with the aid of sticks.

Improvement continued for one month. On June 20 she noticed blurring of vision in the right eye and, within two days, the vision in both eyes had rapidly failed. On June 27 she experienced severe pain in the abdomen with recurrent vomiting. On June 29 the legs became weaker, and on June 30 there was loss of sphincter control. On July 3 she was readmitted to hospital. In addition to the above symptoms she now complained of tingling in the arms. The temperature was 101° F. Both pupils were dilated and responded slowly and incompletely to light. Vision in both eyes was reduced to perception of light. The fundi appeared normal, apart from fullness of the veins. The remaining cranial nerves were normal. There was no loss of power in the upper limbs, or alteration in the reflexes, but thermal and pain sensibility was lost between segments cervical 6 and dorsal 1 on both sides, other forms of sensation being normal. There was complete paraplegia in extension with a well-marked flexion withdrawal reflex. All forms of sensation were lost below the 3rd dorsal segment. On July 5 the loss of thermal and pain sensation extended up to the 4th cervical segment on both sides and both handgrips became weak. On July 8 the arm reflexes were absent, and there was marked weakness of both hands and wrists. On July 7 the dissociated sensory loss was found up to the 3rd cervical on the left side, and power was now diminished at both elbows, and slightly at the shoulders. There was, for the first time, slight postural loss in both hands with diminution of vibration sense, and this loss became complete in the course of the next twenty-four hours. No definite weakness of the diaphragm was apparent. On July 8 she could count fingers with the right eye, but had only perception of light with the left eye. Subsequently complete blindness developed with double optic atrophy. Power partially returned in both arms, but to an insignificant extent in the lower limbs, which passed into paraplegia in flexion. Subsequently there was some return of sensation in the upper limbs, but anæsthesia remained complete on the trunk and lower limbs. Despite an in-dwelling catheter and frequent bladder wash-outs, the urine became heavily infected and she developed bed sores. A lumbar puncture on January 3, 1934, showed 5 cells per c.mm., protein 0·03 per cent., Lange curve normal. She remained totally blind and in a chronic state of paraplegia inflexion. The bed sores extended and she died on August 10, eighteen months after the onset of her illness.

*Case 2.—Female, aged 26, following a cold rapid onset of dorsal myelitis with spread to cervical cord; slow improvement from severe quadriplegia. Nine months after onset bilateral blindness, permanent in right eye. One year later fresh attack of myelitis, rapidly fatal. Duration of illness twenty-six months.*

Dorothy K. On February 29, 1935, when aged 25, she had a tooth extracted under gas and felt indisposed for a few days. On March 9 she developed a cold but no sore throat. During the night of March 13 she began to suffer from a very acute pain in the region of the shoulder blades, and on the morning of March 14 she felt that she had been beaten with sticks across the back. On the morning of March 16, on getting out of bed, she noticed that she could not feel the cold of the linoleum with the left foot. This was succeeded by a dead and heavy feeling which spread up the left leg, and by the following day it had reached the abdomen. On March 18 the right leg felt numb, but she was still able to walk quite well. She noticed slight hesitancy in micturition on this date. On March 20 her legs were weaker and she had retention of urine. The pain had been severe enough to keep her awake at nights, and on the day of admission she had felt an aching pain across the back of the neck. On March 21 she was admitted to the Neurological Ward of the Middlesex Hospital. A striking similarity in facial appearance and colouring between this patient and her sister was noticed. She was equally intelligent, and since she had visited her sister many times in hospital, she was familiar with the symptoms and course of her disease. Yet throughout her own long and distressing illness she displayed the greatest fortitude. Her temperature was normal. The throat was markedly congested. The pupils and fundi were normal. There was no nystagmus and vision was full. The remaining cranial nerves were normal. Power, reflexes and sensation were normal in the upper limbs. The abdominal reflexes were absent. There was a moderate paresis of both lower limbs, more especially of the right one. The deep reflexes were depressed. The right plantar response was extensor, the left equivocal. There was complete loss to pain and thermal sensation on the abdomen below the level of D.6, and on the lower limbs. Tactile and vibration sense in the lower limbs and postural sense in the toes were normal. There was retention of urine. The cerebrospinal fluid was clear. The pressure was 130 mm. of water. Cells 2 per c.mm. Total protein 0·025 per cent. Colloidal gold curve negative. On March 24 the patient appeared drowsy. The temperature was 101·2° F. She complained of pain in both arms and around the neck. There was paresis of both arms, more especially the left. The arm reflexes were increased. There was diminution of pain and thermal sensation in the right arm, and hyperæsthesia in the distribution of the 3rd and 4th cervical segments. On March 27 the pains around the neck were more marked and signs of a paresis of the left cervical sympathetic were noted. No movements of the fingers of the left hand were possible, and those at the elbow joint were weaker, while there was now definite weakness of abduction at the shoulder joint. The same distribution of paresis was present in the right arm, but to a lesser degree. The reflexes in the left arm were diminished. There was a complete flaccid paraplegia of the lower limbs with absent deep reflexes. A definite band of hyperæsthesia was present at the level of C.3. Pain and thermal sensibility were lost below C.3 on both sides, whilst postural and vibration senses were lost on the left hand, but were normal on the right side. All forms of sensation were now lost below D.2.

On April 2 the left arm was completely paralysed, and also the right arm, apart from a feeble movement of abduction at the shoulder. Breathing was mainly carried out by the extraordinary muscles of respiration, although at no time had the diaphragm become completely functionless. Postural loss became complete in the joints of both upper limbs. About a fortnight later power began to return in the arms and proceeded slowly. Pain and thermal sensibility returned rapidly but postural loss and tactile sensation remained impaired in the hands, and did not return until July, 1935. There was no return of power in the lower limbs, and a condition of paraplegia in flexion developed, which was overcome, to a certain extent, by the use of splints. An in-dwelling catheter was used from the beginning and an automatic method of draining the bladder was employed; the urine, however, became heavily infected. Pain and thermal sensibility returned on the trunk and thighs, but remained impaired below the knees. Postural and vibration senses remained lost in the lower limbs. She was discharged to another hospital on September 29, 1935. She was then able to use her hands quite well, but remained completely paraplegic, with no control over her bladder. About December 7 she noticed a large spot in front of the left eye. The vision further deteriorated during the next two weeks. On December 25 she noticed failure of vision in the right eye, which progressed rapidly until she became blind in both eyes. She had experienced no pain in the eyes, or headache.

On January 10, 1936, the patient was readmitted to the Middlesex Hospital. Both pupils were dilated and reacted poorly to light, especially the right. She was able to count fingers with the left eye, whilst with the right eye there was only perception of light. The temporal half of the left disc was pale. The margins of the right disc were fluffy and the veins were engorged. There was a large central scotoma in the left eye. Further improvement in the power of the arms, with slight return of power in the lower limbs, had occurred since her discharge from hospital in October, 1935. There was a marked degree of adductor spasm and a tendency to a paraplegia in flexion. Postural loss was still marked in the distal joints of both feet. There was incontinence of urine with a heavy bacilluria. An indwelling catheter with an automatic washout was again instituted, and mandelic acid given by the mouth. The vision slowly improved in the left eye, so that by the time she was discharged in May, 1936, she could read small print with this eye, but could only count fingers with the right. Both discs were now atrophic. Power had returned sufficiently to the lower limbs to permit of her standing and taking a few steps with support. The bacilluria disappeared, and useful control of the bladder returned, so that she was rarely incontinent. When seen again in September, 1936, she was able to walk alone with the support of two sticks. No further improvement in vision had occurred. She remained in this condition until the beginning of May, 1937, when she complained of pain and numbness around the neck, and she again became incontinent. She was readmitted to the Middlesex Hospital on May 5. She was still able to read small print with the left eye, and count fingers with the right. Both discs were atrophic. There was marked paresis of the left arm and renewed weakness of the lower limbs, left more than right. There was loss of pain and thermal sensibility, and slight impairment of cotton-wool sensation in the distribution of C.3 to 7 on the left side, and on the right arm below C.4. Postural sense in the fingers was intact, and vibration sense was normal. On the trunk there was diminution to all forms of sensation below D.2 on the right side, and D.4 on the left side. She vomited frequently and became drowsy. The

pain around the neck continued. The right arm became paralysed. Postural loss became complete in both arms and pain and thermal loss extended up to C.2. The diaphragm became paresed, and she died of respiratory failure on May 20, twenty-six months after the onset of the disease.

### Pathological Findings.

The usual methods of staining were used in both cases. Sections from various parts of the hemispheres, basal ganglia, brain stem and cord were examined. Unfortunately, the optic chiasma from Case 1 was not available for study.

*Case 1.*—On naked eye inspection of the meninges of the brain and spinal cord, nothing abnormal was noted. However, when the cord was sectioned it was obvious

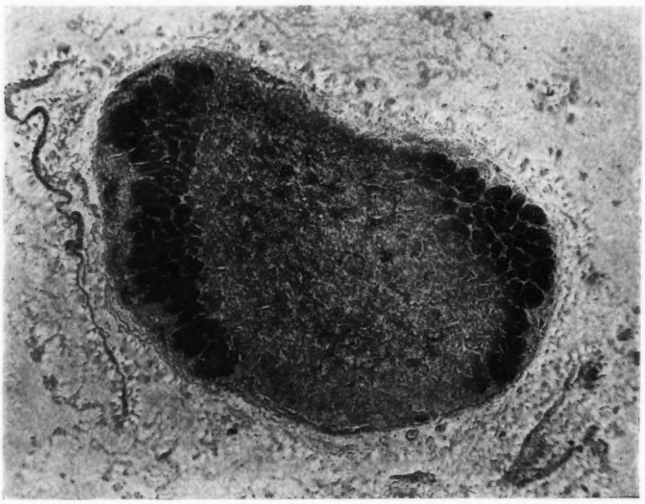


Fig. 1 (*Case 1*).—Diffuse demyelination in centre of optic nerve. Scharlach R. and Hæmatoxylin.

that there was a diffuse pathological process in the mid-dorsal region; there was no differentiation between the white and grey matter, and the cut surface appeared dark brown in colour. Microscopic examination of the cortex, sub-cortical white matter and the basal ganglia, showed no evidence of demyelination or of round-celled infiltration. The mid-brain, pons and medulla were similarly normal. A portion of one optic nerve was available. It showed well marked demyelination in its centre (fig. 1). There was no perivascular or meningeal infiltration. Spinal cord: There was a diffuse demyelination extending from the mid-cervical region to the lower part of the dorsal cord. It was most intense in the cervical enlargement and mid-dorsal region. In the mid-cervical region there was well-marked demyelination of the posterior part of the cord, extending anteriorly to involve both the direct pyramidal tracts, and on one side the antero-lateral part of the cord

(fig. 2). In the upper dorsal cord demyelination extended outwards from the centre of the cord, mainly in an anterior and lateral direction (fig. 3). From the 5th to the 8th dorsal segments there was almost complete demyelination of the whole cord. Normally staining fibres occurred in a few isolated bundles, but the remainder had disappeared. In the lower dorsal and lumbar cord the myelin sheaths showed no appreciable changes, except in the pyramidal tracts, due to a Wallerian degeneration. The axis cylinders showed changes varying from degeneration to destruction in the affected parts of the cord. Perivascular infiltration was conspicuous by its absence throughout the cord and meninges. Microglial reaction was marked in the affected portions of the cord in the form of fat-laden corpuscles and cells with rod-shaped nuclei. Macroglial reaction was moderate considering the age of the lesions. It was slight in the cervical, but somewhat more marked in the mid-dorsal region, more especially towards the periphery of the cord. The blood-vessels showed no evidence of arteritis. There was a slight increase in the number of capillaries in the mid-dorsal region.

FIG. 2 (*Case 1*).—Mid-cervical region (see text). Weigert-Pal.
FIG. 3 (*Case 1*).—1st dorsal segment (see text). Weigert-Pal.

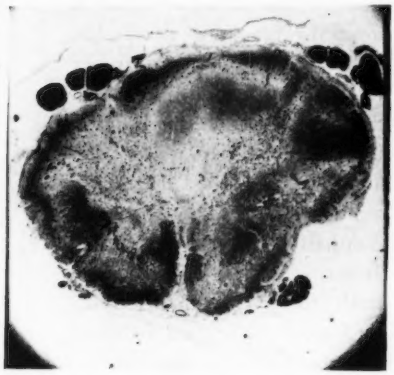
*Case 2.*—The cut surfaces of the cord showed a greyish softening from the cervical region to the middle of the dorsal cord, similar to that observed in Case 1, but more marked in degree. The histological changes were confined to the optic chiasma, optic tracts, optic nerves and to the spinal cord. No demyelination or perivascular infiltration was observed in sections from various parts of the cortex, basal ganglia, ventricular walls and brain stem, with the exception of the lower medulla, where two small recent areas of demyelination with round-celled infiltration were found in its dorsal part. The optic chiasma was cut in serial sections. A diffuse demyelination was present extending into both optic nerves and the left optic tract. The demyelination at certain levels was not complete and bundles of normally staining fibres were present (fig. 4). The majority, however, showed changes varying from complete disappearance to fragmentation and ballooning. In the centre of the chiasma, in the more caudal sections, the process had advanced to necrosis. With the exception of a small, rather sharply delimited, area in the right optic tract, the demyelinating process was a diffuse one. Perivascular infiltration

on the whole was slight; when present, the cells were mainly fat granule corpuscles, with a few lymphocytes. Sections of the optic nerves showed a diffuse demyelination at the centre of each nerve. Spinal cord: There was a diffuse demyelination extending from approximately the 2nd cervical segment to the 10th dorsal segment. The process was most intense in the cervical enlargement, and the mid-dorsal region. In the cervical region demyelination diffusely affected the cord, sparing only the anterolateral tracts on one side. From segments C.5 to 8 there was necrosis and cavitation in the centre of the cord. In the 1st and 2nd dorsal segments the process was more widespread than in the cervical cord, being especially intense in the centre of the cord, where it extended outwards, only

FIG. 4 (*Case 2*).—Optic chiasma (see text). Weigert-Pal.

sparing parts of the anterolateral tracts (fig. 5). From the 4th to the 6th dorsal segments the lesion was at its maximum; demyelination was complete, except for a few scattered bundles of fibres. The centre of the cord was necrotic (fig. 6). At the level of the 8th dorsal segment demyelination was less complete, being more marked in the posterior than in the anterior half of the cord. Degeneration of the pyramidal tracts was symmetrical. In the lower dorsal and lumbar cord there was a descending degeneration of the pyramidal tracts. The axis cylinders were considerably affected, especially in the cervical and mid-dorsal regions. Many of the fibres seemed to have been destroyed, whilst others showed gross changes including fragmentation, swelling and end bulb formation. In the less affected areas many of the axis cylinders were normal. Microglial reaction was marked; fat granule corpuscles were abundantly present in the affected portions of the cord. Cells with rod-shaped nuclei were more frequent at levels where the lesion was moderate or slight in degree. Macroglial reaction was poor; gliosis on the whole was conspicuous by its absence. In the mid-dorsal region, where the necrotic process was most marked, a few astrocytes were seen situated at the periphery of the cord; the majority shewed degenerative changes such as swelling of the cell body. Perivascular infiltration was marked in the cervical cord, more especially around the branches of the anterior spinal artery. The cells were mainly lymphocytes. There

was a moderate meningeal reaction. Similar changes, though more marked, were present in the mid-dorsal region. On the other hand, the vessels and meninges of the lumbar cord were normal. The grey matter was considerably altered at certain levels, especially in the mid-dorsal region. No trace of the anterior horn cells remained. In the cervical cord the cells that were present shewed chromatolytic changes. A striking feature in the mid-dorsal region was a marked increase in the number of thin-walled capillaries. No evidence of an arteritis was found. Fibroblastic reaction was comparatively mild.



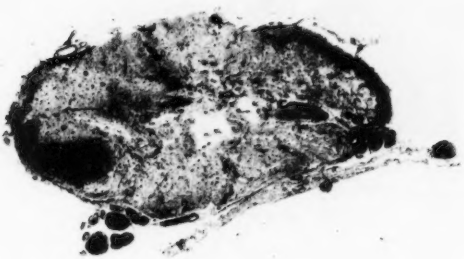


Fig. 5 (*Case 2*).—2nd dorsal segment. Diffuse demyelination. Weigert-Pal.

Fig. 6 (*Case 2*).—6th dorsal segment. Diffuse demyelination with necrosis and cavitation in the centre of the cord. Weigert-Pal.

## A Comparison of the Two Cases.

The clinical picture on the whole was strikingly similar in these twins. In each a " cold " preceded the first symptom of myelitis. Severe pain across the upper back, tingling and numbness in the left leg ascending to the abdomen and then affecting the right leg, was the sequence of the sensory disturbance in both cases. Each patient was admitted on the tenth day of her illness and each showed signs of a severe mid-dorsal myelitis. In both cases the right leg was weaker than the left. In Case 1 thermal and pin-prick sensation were at first only lost on the left leg, whilst in Case 2 the initial sensory loss on both lower limbs was confined to these forms of sensation. The rest of the examination of the nervous system, including vision, was negative in both cases at this stage. The cerebrospinal fluid was normal throughout the illness in both cases, except that on the first occasion Case 1 showed a mild Lange colloidal gold curve. The course of the disease was now different. In Case 1 the myelitic process, although becoming

more severe, remained localised to the dorsal cord. Slow improvement occurred and four months later she was discharged from hospital able to walk a little and having regained to a large extent control of her bladder. In Case 2, within three days of admission the cervical cord became affected. It is interesting to note that thermal and pin-prick sensation were affected in the right arm, whilst other forms of sensation remained normal for a few days. This patient passed through a stage of quadriplegia, but subsequently power began to return in the upper limbs, but scarcely at all in the lower limbs, even after six months in hospital. Blindness marks the next phase of the disease in both cases. In Case 1, one month after her discharge from hospital and five months after the onset of the illness, loss of vision was noticed, first in the left eye ; within one week she was blind in both eyes except for the perception of light. In Case 2, ten weeks after leaving hospital and nine months from the onset, vision failed in the left eye, and eighteen days later in the right eye. The third phase in each case was a fresh myelitis. In Case 1 this accompanied the onset of blindness, a fresh dorsal myelitis occurring which spread to the cervical cord, resulting in a quadriplegia which became chronic, the patient finally dying of bed sores and a severe bladder infection. In Case 2 the second attack of myelitis did not occur until a year later ; it affected the cervical cord and rapidly proved fatal. If these events are summarized in the two cases, it will be seen that in Case 1 the duration of the illness was eighteen months, and in Case 2 twenty-six months. In both cases there were two distinct attacks of myelitis. In both cases the ocular symptoms and signs were very similar, failure of vision beginning in the left eye, and later going on to blindness. In Case 1 there was no appreciable return of vision, whilst in Case 2 vision in the left eye returned sufficiently to enable the patient to read. Both cases shewed a central scotoma initially. In Case 2 there was an unilateral papillitis. The final picture in both cases was one of optic atrophy.

The pathological process in both cases was limited to the cord, optic chiasma, optic tracts and optic nerves. No change of importance was found in the cerebral hemispheres, in the walls of the lateral ventricles or in the brain stem, with the exception of two recent areas of demyelination in the dorsal part of the medulla in the second case. The optic nerve in Case 1 shewed well-marked demyelination. In Case 2 there was a diffuse demyelination of the optic chiasma, optic nerves and the initial portion of one optic tract. In both cases there was a diffuse myelitis extending from the cervical region through approximately two-thirds of the dorsal cord. In both cases the macroscopic appearance of the cord was striking. In the

mid-dorsal region, over several segments, the cut surface of the cord appeared dark brown in colour. The substance of the cord was soft and diffluent, and there was no distinction between the white and grey matter. In the cervical cord demyelination in both cases affected particularly the dorsal half of the cord, the process spreading outwards from the region of the central canal. In the mid-dorsal region demyelination was nearly complete in both cases. In the cervical enlargement in Case 2 and in the dorsal cord in both cases, the process had advanced to necrosis. In Case 2 atrocytes were scarce, except at the periphery of the cord, and gliosis was absent or slight. In Case 1 the macroglial response was more definite, especially in the less affected portions of the cord. In both cases there was a brisk microglial response in the form of fat-laden corpuscles and cells with rod-shaped nuclei. Perivascular and meningeal infiltration with lymphocytes was evident at most levels of the cord in Case 2, but was absent in Case 1. The anterior horn cells in the cervical and dorsal cord shewed changes ranging from complete destruction to varying degrees of chromatolysis. Capillary overgrowth was a feature of Case 2, but was slight in Case 1.

## Discussion.

*Clinical diagnosis.*—Neuromyelitis optica, though somewhat variable in its effects on the nervous system, shows certain distinctive features. The age incidence varies from five to over sixty years; the disease is, however, commoner in the early decades of life. Constitutional symptoms are not uncommon at the onset, especially headache, sore throat and a raised temperature. After an interval of a few days, or, more rarely, several weeks, the first symptoms of invasion of the central nervous system shew themselves. According to Beck (1927) 75 per cent. of cases shew failing vision as the first sign of the disease, and subsequent writers agree that this is the usual mode of onset. In the remaining cases, symptoms of a myelitis are the first to declare themselves. Where blindness first appears, signs of a myelitis may follow at an interval of some hours, weeks, or rarely, months. The same intervals may occur between the myelitis and the first signs of failing vision. Blindness may be first noticed in both eyes, or affect each eye at an interval of a few days, or rarely, two or three weeks. As a rule the failure of vision is extremely rapid, so that in a few days there may remain only perception of light. In such cases the pupils are usually dilated and react sluggishly to light. The discs may be normal, or there may be a papillitis, unilateral or bilateral. Vision may be so reduced that charting of the visual fields is impossible. Where the loss of vision is less sudden or less complete it is usually possible to establish the presence of a large

central scotoma. Homonymous defects may co-exist, or at first constitute the only perimetric change. Partial recovery of vision may occur, especially in those cases that survive some weeks or longer. This recovery may be unilateral or bilateral. In other cases varying degrees of blindness remain. The discs in the later stages are atrophic. Diplopia and nystagmus are conspicuous by their absence. It is true that in isolated cases these signs have been observed, but their continued presence should throw doubt upon the diagnosis of neuromyelitis optica. In the majority of cases the dorsal portion of the cord is first attacked. Pain is commonly the earliest symptom, being referred to the back, between the shoulders, in a girdle distribution, or in the legs. It is frequently described as sharp or shooting and may be severe. Numbness and tingling are the usual forms of paræsthesiæ which follow in either one or both lower limbs, spreading upwards to the abdomen. Within a few hours or days weakness of the lower limbs is noted, and retention of urine follows. In the acute cases the deep reflexes are depressed or absent, whilst in those cases in which the onset is more insidious they are exaggerated from the commencement. Muscular wasting has been reported, usually in the upper limbs, in a few of the more chronic cases. Sensory loss as a rule does not differ from that found in other forms of acute myelitis. In the initial stages the upper level of sensory loss usually lies between the upper and mid-dorsal regions. There may be a zone of hyperæsthesia. In both the cases reported in this paper there was an initial stage in which pain and thermal sensibility were alone affected for a few days. A similar dissociated loss has been observed in other cases. |Balser (1936), Milian, Lhermitte, Schaeffer and Horowitz (1931), Dollfuss (1928).| This stage is only a temporary one and is followed by loss of tactile and deep sensation. With rare exceptions the disease spreads to the cervical cord. In the rapidly progressive cases this extension occurs at a short interval after the first sign of the dorsal myelitis. Death usually takes place as a result of respiratory failure, more frequently from paresis of the phrenic nerve than from extension of the process to the medulla. Temporary recovery is possible even after involvement of the cervical cord, as evidenced by Case 1. In the more chronic type of case, with remissions, an interval of weeks or months may elapse before the cervical cord is affected. Emphasis has already been laid on the rarity of nystagmus and diplopia in this disease. In addition to these, euphoria, paresis of cranial nerves (with the occasional exception of the 10th), tremor or ataxia, do not occur, even in the more chronic cases.

*Cerebrospinal fluid.*—Certain characteristic findings occur. In over 50 per cent. of cases, and in a higher percentage in the rapidly progressive

type, there is an increase in cells, mainly polymorphonuclear in type. The protein is moderately raised. The Lange and benzoin curves are almost constantly negative in all stages of the disease. This association of a cell increase and a negative colloidal curve would appear to be characteristic of neuromyelitis optica.

Of the cases occurring since the publication of Beck's (1927) paper twenty-two cases, including the two described in this paper, have been analysed as to their course; they would appear to fall into three groups. (1) Those cases which follow a progressive course, death occurring in from five days to several weeks. Ten of the cases came into this group. (2) Cases which shew one or more remissions, but finally die after some months up to two or three years. There were seven cases that followed this course. (3) Cases which recover completely or partially, of which there were five examples. It is doubtful whether these cases have been followed sufficiently long to justify a diagnosis of neuromyelitis optica: some of them may eventually prove to be suffering from disseminated sclerosis.

*Pathological diagnosis.*—Neuromyelitis optica is characterized by a severe demyelinating process which affects the optic chiasma, optic nerves, optic tracts, and the spinal cord. There is a relative escape of the brain and brain stem. Beck, in 1927, collected twenty-five cases in which pathological examinations had been performed. Nine of these showed disseminated foci, whilst in sixteen there was evidence of a diffuse myelitis. The present writer has collected a further twelve pathological reports since the publication of Beck's paper, including the two cases which are the subject of the present paper. In nine of these the myelitis was diffuse, whilst in the remaining three there were disseminated foci. A diffuse demyelination would therefore appear to be the characteristic lesion in neuromyelitis optica. A further hallmark of the disease is necrosis, sometimes accompanied by cavitation: this occurs almost constantly when the myelitis is diffuse. On the other hand, those cases in which there are disseminated foci seldom show this change. There is considerable variation in the histological details in this disease. This is understandable when such factors as the varying duration of the illness, and, in the chronic cases, the absence or presence of an exacerbation of the disease shortly before death, are considered. The following summary is based upon twelve recently published cases. In the areas most affected, more especially in those that are necrotic, destruction of axis cylinders is usual. Of those that survive, the majority shew degenerative changes, whilst a few remain unaltered. When the myelitis is less intense the axis cylinders are less altered, and some may be normal. As might be expected from the variation in the intensity and

duration of the morbid process, the response of the neuroglia is inconsistent. Of three cases reported by Balser, in only one of them was the glial proliferation more than slight. In a case reported by Hassin (1937), astrocytes were comparatively scarce, chiefly occurring at the edge of the affected areas. The fibrous astrocytes were especially rare and often shewed a breaking up of their processes. Marchiewicz and Peters (1936) and Gozzano (1937) comment on the relative absence of gliosis. On the other hand, Milian and his collaborators (1931) report a case in a male aged 37 in whom death occurred at the end of five weeks. Disseminated foci were found in the cord and chiasma. None of the lesions were necrotic. There was a definite increase of macroglial elements. These authors believe that in this case there was a double process, destructive and reactional, resulting in a hyperplasia of the macro- and micro-glial elements. Cestan, Riser and Planques (1934) have reported a case in a male aged 50 who suffered from hypertension. He developed an aphasia and later a quadriplegia which improved. This was followed by failure of vision with papillitis. Again there was improvement. The patient died finally from uræmia eleven months after the onset. Several thrombotic softenings were found in the brain, and in addition disseminated foci, greyish in colour, which the authors consider to be precisely the same as those found in disseminated sclerosis; none of these shewed necrosis. There was a marked increase in the number of astrocytes. This case is atypical, not only because of the co-existence of cerebral vascular disease, but also by the occurrence of foci of demyelination in the brain stem and hemispheres. In both these cases there were disseminated foci and necrosis had not occurred. It would seem to the writer that the variations in the response of the macroglia in this disease to a large extent depend upon the intensity of the lesion. When necrosis occurs the astrocytes are not even spared, and therefore a subsequent gliosis is not possible, except at the margins of the affected areas. On the other hand, the microglia uniformly show a marked reaction, more especially in the form of fat-granule corpuscles; their other derivative, namely, cells with rod-shaped nuclei, are scarce in the necrotic areas, but are plentiful where the process is less acute. With regard to evidence of an inflammatory reaction, here again the findings vary considerably. In Balser's first case, perivascular infiltration with lymphocytes and plasma cells was found, especially in the chiasma. The duration of the illness was nine weeks. In his second case, which lived for five months after the onset, a similar degree of inflammatory reaction was found. In the case reported by Uréchia and Veluda (1934) in which death occurred in the short time of five days after the appearance of the first symptom, a diffuse inflam-

matory lesion, especially in the neighbourhood of blood vessels, was present throughout the cord, chiasma, and optic nerves. The meningeal vessels were infiltrated with polymorphonuclears, lymphocytes, and plasma cells. In the chronic relapsing type of case evidence of any inflammatory change may be slight or absent, as in a case reported by Hassin, and in the two cases described in the present paper, in the second of which mild inflammatory changes could be explained by a recent exacerbation shortly before death. It would appear that a true inflammatory reaction usually occurs in the acute phases of the disease, but is slight or absent in the more chronic cases. The grey matter may be affected as much as the white matter, and several of the reported cases have shewn destruction of anterior horn cells when the lesion has been severe. There seems a predilection for the central grey matter to be particularly affected, and it is in the region of the central canal that cavitation may occur. A considerable increase in the number of capillaries has been noted by Balser in two of his three cases, and by Hassin and Beck. It was a feature of Case 2 in this paper. Such changes, however, seem to be relatively uncommon. Two conditions seem necessary for this change. Firstly, a duration of the illness for some months: for example, in Hassin's case, which lived for fifteen months, the capillary overgrowth, judging from the illustration in his paper, was as well-marked as in the present Case 2, who lived for twenty-six months. Secondly, in all the cases in which this feature has been present, necrosis of the cord has occurred. It would seem logical to assume that the destruction of astrocytes, which results from the necrosis, and the consequent poor glial reaction, leaves only one tissue in a position to effect repair, namely the blood vessels. At the same time, one would have also expected a marked fibroblastic reaction. This, however, occurs less frequently than the capillary overgrowth, although in a few cases it has been marked. (*See* Balser, Case 3.)

The relationship of neuromyelitis optica to the other demyelinating diseases must remain uncertain until more is known of their ætiology. The present writer shares the view of those who hold that in neuromyelitis optica there are certain clinical and pathological features which distinguish it from other members of the demyelinating group. Neuromyelitis optica is characterized by the combination of severe visual and spinal cord symptoms and signs. These may occur concurrently, or may follow one another at a short or a long interval. Signs of involvement of the brain stem are conspicuous by their absence. The cerebrospinal fluid may be normal, or may show an increase in cells and protein with a normal colloidal gold or benzoin curve. The course of the disease is progressive or remittent, but death occurs in the majority of cases within two years. Recovery,

usually with sequelæ, seems possible in a small number of cases. The characteristic pathological feature of the disease is a diffuse demyelinating process, often going on to necrosis, which attacks the optic chiasma, optic nerves and spinal cord, with a relatively poor glial fibre reaction. More rarely there are foci of demyelination which do not show necrosis, and in this type of case the glial reaction may be quite marked. Apart from the rare occurrence of discrete demyelination in the brain stem and an occasional vessel showing perivascular infiltration, there and in the basal ganglia, the rest of the nervous system shows no notable pathological change. If these criteria, clinical and pathological, be applied, then it is possible to regard neuromyelitis optica as an entity distinguishable from the other demyelinating diseases such as Schilder's disease, acute disseminated encephalomyelitis and disseminated sclerosis, in all of which visual loss associated with a myelitis may occur. It is natural to suppose that cases from each of these groups will occasionally be encountered which show features common to more than one of them. For example, the clinical and pathological picture of Schilder's disease is so different from that seen in neuromyelitis optica that no confusion would seem possible. However, in the following case reported by Marinesco, Draganesco, Sager and Grigoresco (1930), there were features common to both conditions. The case was that of a woman aged 21 who, in January, 1929, developed headache and vomiting and pain in the lower limbs, followed a month later by double vision, and later by bilateral blindness. In April there was a rapid development of a right-sided hemiplegia with dysarthria, which improved in the course of a few days. In May, she showed signs of a flaccid paraplegia with retention of urine. The cerebrospinal fluid was normal in all respects. The patient died six months after the onset. The cord showed softening from the 5th to the 9th dorsal segment. The right hemisphere showed no lesion. The left hemisphere showed two extensive areas of degeneration, greyish-yellow in colour, and spongy in consistency. They were both confined to the white matter. The one occupied the white matter of the occipital lobe with an extension towards the occipital horn of the lateral ventricle, and even invading the left half of the splenium of the corpus callosum. The other lesion was situated in the centrum ovale beneath the parietal and ascending frontal convolution. The chiasma showed extensive demyelination of its central portion, and in addition there was demyelination close up to the nerve head on the left side. The author's comment on certain features of the case which are characteristic of Schilder's disease, the hemiplegia and the distribution of the lesion in the left hemisphere, although an unilateral effect, is

unusual in this disease. The occurrence of a myelitis suggest neuromyelitis optica, and the pathological findings in the chiasma and left optic nerve also favour this diagnosis. They comment on the rarity of spinal cord lesions in Schilder's disease, but refer to the case published by Stewart, Greenfield and Blandy (1927), where cord lesions were found. The authors find in their case a link between neuromyelitis optica and Schilder's disease, but consider that their case comes into the category of neuromyelitis optica. Until we have further knowledge of the ætiology of the demyelinating diseases, it may be impossible to classify such a case as this one.

Certain of the acuter cases of disseminated sclerosis may resemble neuromyelitis optica. However, disseminated sclerosis is as a rule more widespread through the central nervous system, giving rise to a variety of signs that are usually absent in neuromyelitis optica, such as euphoria, ocular pareses, nystagmus, and the other signs associated with disturbance of the cerebellar and vestibular connections. Although loss of vision occurring in both eyes simultaneously does occasionally occur in disseminated sclerosis, recovery as a rule is more complete than in neuromyelitis optica. In the few instances of disseminated sclerosis personally observed where there has been a degree of permanent blindness in both eyes, the defect has always been in the nature of a large central scotoma, no permanent hemianopic loss such as may occur in neuromyelitis optica having been observed. Neuromyelitis optica tends to produce symmetrical effects on the central nervous system. It is true that at the onset one eye and one lower limb may be affected, but in the course of a few hours, or days, the other eye and leg are involved. This symmetrical picture is explained by the tendency of the pathological lesion to be a diffuse one. In disseminated sclerosis, on the other hand, the disease is frequently asymmetrical in its effects, loss of vision being confined to one eye, or, in a paraplegia, one lower limb may be more paresed than the other. As a rule acute cases of disseminated sclerosis shew a greater capacity for recovery than do cases of neuromyelitis optica, as Brain (1933) has pointed out. Merritt (1934) has analyzed the cerebro-spinal fluid findings in 839 cases of disseminated sclerosis. Seventy-one per cent. showed an abnormal Lange colloidal gold curve. In neuromyelitis optica, on the other hand, the Lange curve is almost constantly normal, despite a not infrequent pleocytosis. It must be admitted, however, that cases are encountered from time to time which show features suggestive of both conditions. For example, instances of acute bilateral retrobulbar neuritis associated, perhaps, with a papillitis, but with no other evidence of disease of the central nervous system, are occasionally encountered. Rarely, an infection of the nasal sinuses may

be present to explain the condition. In the remainder the diagnosis would seem to lie between disseminated sclerosis and neuromyelitis optica, although it is possible that a few of these cases may never show any further evidence of disease of the central nervous system. A considerable return of vision and a positive colloidal gold curve in such a case would point to disseminated sclerosis. In other cases no definite conclusion may be reached during the life-time of the patient, although the course of the disease, its distribution in the nervous system as judged by the signs, the frequency of relapses and the degree to which they remit, and, lastly, the findings in the cerebrospinal fluid, may enable a conclusion to be arrived at. Finally, the possibility of death occurring in neuromyelitis optica from a myelitis, before the disease has attacked the chiasma, must not be lost sight of.

There are certain differences in the pathological picture which would strengthen the belief that neuromyelitis optica and acute disseminated sclerosis are separate conditions. As a rule the morbid process is more intense in neuromyelitis optica, necrosis being a relatively common finding, whilst its presence in disseminated sclerosis is quite exceptional and probably an accidental finding. From these facts it is only to be expected that there should be differences in the final histological picture in the two diseases. In disseminated sclerosis there is little tendency for destruction of axis cylinders, although they may undergo degenerative changes, whereas in neuromyelitis optica they may be destroyed. In disseminated sclerosis gliosis is a feature of the disease, whereas in neuromyelitis optica the poor response of the macroglia can be attributed to the destruction of astrocytes in the necrotic process. When gliosis is marked, as a rule, the initial lesion has not been so severe. In neuromyelitis optica the grey matter may be as severely affected as the white matter. As Hassin points out, in disseminated sclerosis there may be cellular infiltration of the anterior horns, but the cells themselves are spared, whereas in neuromyelitis optica they are often destroyed. Lastly, an increase in capillaries, which may occur in certain of the more chronic cases of neuromyelitis optica, is not met with in disseminated sclerosis.

Acute disseminated encephalomyelitis, whether spontaneous or following one of the infectious fevers, shows a clinical picture which, in many respects, is different from that seen in neuromyelitis optica. The lesions are more widespread, and may occur through the hemispheres and brain stem, thus giving rise to signs which do not occur in neuromyelitis optica. Most authorities are agreed that blindness is rare in this condition. The pathological picture is one of scattered foci, of demyelination throughout

the nervous system with a distinctly perivascular distribution. Hassin stresses the widespread inflammatory features met with in acute disseminated encephalomyelitis.

Returning to the two cases described in this paper, in Case 1 the diagnosis for a time was in doubt. The patient was shown at a meeting of the Neurological Section of the Royal Society of Medicine under the title "Myelitis with Blindness: Acute Disseminated Encephalomyelitis." The clinical picture, the course of the illness, and the results of the pathological examination, are so similar in the two cases, that there can be no doubt that they were affected by the same disease. Judged by the criteria discussed in the previous paragraphs, a diagnosis of neuromyelitis optica seems justified. Speculation as to the reason why these identical twins should suffer the same rare disease of the nervous system is scarcely warranted, in view of our ignorance as to its causation. Assuming, however, that the changes in the nervous system in neuromyelitis optica are due to a virus or its toxin, two possibilities suggest themselves: (1) That each of them had harboured the virus for some years before the nervous system was attacked; or (2) that Case 2, who frequently visited her sister during the latter's illness, was infected by her. It seems likely that if a lowered resistance to disease of the nervous system was inherited, it would be shared by both, in view of their relationship.

I am indebted to Professor J. McIntosh for the facilities he afforded me in the Bland-Sutton Institute of Pathology.

SUMMARY.

(1) The clinical and pathological features of neuromyelitis optica as it occurred in identical twins are described.

(2) These two cases support the view that there is sufficient justification for regarding neuromyelitis optica as a distinct member of the demyelinating group of diseases.

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# DISTURBANCES OF SENSIBILITY IN DYSTROPHIA MYOTONICA.

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In the majority of accounts of dystrophia myotonica nothing is said with regard to sensibility in this malady. Curschmann (1936) states that no disturbance of sensibility is to be observed. Rouquès (1931) recorded sensory changes as a rare, and, as he thought, an unimportant exception.

During the course of a study of dystrophia myotonica, the present writer found on the routine testing of vibration sense by the tuning fork that, as compared with the normal subject, this mode of sensibility seemed sometimes impaired in the subject of dystrophia myotonica. However, the absence of satisfactory quantitative standards of acuity of this mode of sensibility made the evaluation of this observation difficult. A quantitative investigation was therefore attempted, and its results are here recorded.

*Method of examination.*—An apparatus devised by Newman and Corbin (1936) was employed. It consists of an electromagnetic vibrator with a frequency of 300 cycles per second. By means of suitable meters, the threshold of vibration perception in milliwatts can be recorded, the instrument resting by its own weight on chosen sites: namely, the ulnar styloid process, the tibial tuberosity and the internal malleolus.

In the subjects examined the observations were made for me with this instrument by Dr. H. W. Newman, to whom I express my warmest thanks.

*Observations and results.*—A normal standard was obtained by a series of observations upon eight healthy subjects ranging in age from 26 to 34 years.

In a series of twenty-two patients suffering from dystrophia myotonica, their ages ranging from 13 to 35 years, fourteen showed an acuity of vibration sense less than that of the least acute normal control. This impairment was greatest at the wrist and less at knee and ankle.

Six patients suffering from dystrophia myotonica between the ages of 49 and 55, when compared with a single normal control aged 63, all showed vibratory acuity less than a third of normal at the wrist, while three of them showed diminished acuity at ankle and knee as well.

TABLE

| | Name | Sex | Age | Vibration-sense | | | Myotonia | Muscle-atrophy |
|---|---|---|---|---|---|---|---|---|
| | | | | Ulna | Tibia | Malleolus | | |
| 1 | D.-B. | Female | 26 | — | — | — | Mild | Mild |
| 2 | F. F. | Male | 33 | — | — | — | Mild | Mild |
| 3 | D. J. | Female | 18 | — | — | — | Doubtful | Doubtful |
| 4 | T. W. | Female | 21 | — | — | — | Marked | Marked |
| 5 | T. B. | Female | 22 | — | — | — | Mild | Mild |
| 6 | G. B. | Male | 24 | — | — | — | Mild | Mild |
| 7 | A. B. | Male | 28 | — | — | — | Marked | Mild |
| 8 | T. B. | Male | 25 | — | — | — | Mild | Mild |
| 9 | R. G. | Male | 32 | XXX | X | XXX | Marked | Marked |
| 10 | G. J. | Female | 17 | XXX | X | X | Mild | Mild |
| 11 | G. C. | Female | 21 | XXX | — | X | Mild | Mild |
| 12 | L. F. | Female | 27 | XXX | X | X | Mild | Mild |
| 13 | F. J. | Male | 26 | XXX | X | — | Mild | Mild |
| 14 | B. J. | Male | 24 | XXX | XXX | XX | Mild | Mild |
| 15 | C. D. | Male | 35 | XXX | XXX | | Mild | Mild |
| 16 | J. M. | Male | 28 | XXX | XXX | X | Very marked | Very marked |
| 17 | J. G. | Male | 35 | XXX | — | — | Very marked | Mild |
| 18 | D. D. | Female | 25 | XXX | — | — | Doubtful | Doubtful |
| 19 | F. H. | Female | 19 | XXX | XXX | XXX | Doubtful | Doubtful |
| 20 | E. H. | Female | 22 | XXX | X | X | Doubtful | Doubtful |
| 21 | L. R. | Female | 13 | XX | X | X | Mild | No atrophy |
| 22 | H. C. | Male | 35 | XXX | XX | XX | Marked | Marked |

The sign — denotes vibratory-acuity within normal limits; X, decreased up ½ of normal; XX, from ½-¼ of normal; XXX, less than ¼ normal acuity.

No constant relationship was found between the severity of myotonia and muscular wasting on the one hand, and the presence or degree of impairment of vibration sense on the other. Of the 22 subjects in the table only three (2, 7, 17) were in hospital on account of weakness or myotonia, the remainder were discovered in the course of a routine investigation of families of persons suffering from dystrophia myotonica and in hospital for this reason.

It appears then that in this series of myotonic subjects about two-thirds presented signs of impaired vibration sense. In all these, routine investigation of cutaneous sensibility (tactile and painful) revealed no abnormality. The subsequent examination of three subjects suffering from well-developed dystrophia myotonica and impairment of vibration sense revealed a normal threshold of tactile sensibility to testing with von Frey's hairs, and a normal threshold to cutaneous pain sense.

At what point in the sensory pathway the conduction of impulses subserving the vibration sense is interfered with is not known. So far, histological examination of the nervous system in dystrophia myotonica has thrown no light on this point. Steinert (1909) reported degeneration in

the posterior columns of the cord in one case. In two cases some degeneration of the nerve cells was found in the lateral cell column in which the spinocerebellar tract is believed to arise, but the fibres of this tract were not degenerated, and no relation can be established between this nerve cell lesion and impairment of vibration sense. (Bielschowsky, Maas, Ostertag, 1933.) (Keschner and Davison, 1933.)

Dr. Greenfield kindly examined histologically a cutaneous nerve removed during life from the outer side of the foot in a subject with impaired vibratory acuity at the ankle and suffering from dystrophia myotonica. The examination revealed a perfectly normal nerve.

Although in the series already discussed no impairment of any mode of cutaneous sensibility was observed, the routine examination of a large number of cases of dystrophia myotonica did reveal abnormalities in seven instances. These consisted in areas of tactile hypæsthesia, hypalgesia to pin-prick, or of hypotherm-anæsthesia—either associated or separately—in the distal segments of the limbs. In some cases the entire hand was thus affected. These changes were not of severe degree. Many of these examinations were made under unfavourable conditions, as for example in the patients' homes, and it is possible that more rigorous investigation might reveal a greater frequency of these sensory abnormalities than has been found.

A review of the literature of the disease yields numerous passing references to sensory anomalies. Thus, the presence of spontaneous pains and of paræsthesiæ (" pins and needles ") are recorded by Rossolimo (1902), Pelz (1907), Batten and Gibb (1909), Buzzard (1909), Hirschfeld (1925), Bregman and Potok (1932), Curschmann (1936). Pelz also cites other writers in his paper.

Hypoæsthesia to pressure is recorded by Baake and Voss (1917), Rossolimo (1902) and Pelz (1907).

Diminished sensibility to touch, pain and thermal stimuli, either singly or together, are recorded by Curschmann (1936), Nischau (1920), Scharnke and Full (1920), Steinert (1909), Berg (1904), Gökay (1936), Lortat-Jacob and Thaon (1905).

Disturbance of postural sensibility is recorded by Curschmann (1936) and Rohrer (1916).

This list is probably incomplete, but the results of my own examinations together with the references given suggest that the view held by some authors that these sensory changes are hysterical in nature is not tenable.

Whether these changes derive from peripheral or central nervous changes cannot be determined in the present state of knowledge.

## Conclusion.

Disturbance of vibration sense is a sign observed in many cases of dystrophia myotonica. In consequence of its frequency we may regard it as an integral part of the symptom complex.

Other signs of disturbed sensibility arise much less frequently. However, they occur in a sufficient number of cases to make it unlikely that they are the result of any affection complicating dystrophia myotonica.

The frequency of signs of sensory change in dystrophia myotonica suggests that this malady is not solely the result of an affection of the muscles themselves.

The author expresses his thanks to the honorary staff of the National Hospital, Queen Square, and to Dr. W. A. Spence of St. Bartholomew's Hospital for permission to examine the cases which form the basis of this paper.

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## Notices of Recent Publications.

*Meningiomas: Their classification, regional behaviour, life history, and surgical end results.* By Harvey Cushing, with the collaboration of Louise Eisenhardt. Baltimore: C. H. Thomas. 1938. Pp. 785. Figs. 685.

The differential diagnosis, pathological and topographical, of intracranial tumours has made remarkable strides in the last few years, and no student of the subject can be unaware of the share in this progressive refinement of diagnosis that neurologists owe to Harvey Cushing and his collaborators. A steady flow of monographs and papers have come to us from this source, and the present exhaustive analysis of the symptomatology, behaviour and treatment of the meningiomas is a worthy member of a unique series. The complete and orderly presentation that the reader has learned to expect from Harvey Cushing is here, and proves—if proof were needed—that the field of clinical observation still offers a rich harvest to those who work in it.

*The Physiology of the Nervous System.* By J. F. Fulton. London: Oxford Medical Publications. 1938. Pp. 630. Figs. 94. Price 25s.

This book is addressed to students of medicine "who must bridge the gap between the concepts of neurophysiology and the problems of clinical neurology."

It may truly be said that the facts of clinical observation for the seeing eye often throw light upon the normal physiology of the nervous system, and in so doing amplify and extend the experimental work of the physiologist. Any exposition of neurophysiology that will facilitate this process will be valuable to workers in both fields, but we may in this connexion more accurately speak of co-ordinating these two orders of observation than of bridging gaps.

Of its nature the task that the author has courageously undertaken is as difficult for the physiologist as for the clinician. The former is writing for someone with whose problems he has no first-hand acquaintance and cannot therefore achieve the selection of what is relevant and useful, nor present this in the most appropriate manner and with the proper emphasis. The latter lacks the personal experience of experimental methods and of the reactions of the experimental animal which are necessary if he is to assess and apply what the physiologist has to tell him.

In the writing of such a book the counsel of perfection indicates a collaboration between physiologist and clinical neurologist, and we may regret that Professor Fulton has not availed himself of a collaboration of this order, for it was surely available.

The lack of it is most clearly seen in the remote and inadequate treatment of the physiology of sensation, but it is evident here and there throughout the book.

Nevertheless, this may be used as a quarry from which the neurologist may dig what he wants, and in his search he is aided by a vast bibliography of some 1,300 papers and a number of clear diagrams.

*The Pituitary Gland: An investigation of the most recent advances.* Association for Research in Nervous and Mental Diseases. Volume XVII, 1938. London: Baillière, Tindall, and Cox. Pp. 764. Figs. 160 and 50 Tables. Price 45s.

The scope and plan of this volume will be familiar to those who have seen its predecessors in the series. It is divided into three sections, anatomical, physiological and clinical, and provides an exhaustive summary of present knowledge of its subject. Each chapter is followed by a bibliography.

*Das Zwischenhirn und die Regulation von Kreislauf und Atmung. Beiträge zur Physiologie des Hirnstammes.* II ter. Teil. By W. R. Hess. Leipzig: G. Thieme. 1938. Pp. 125. Price RM. 32.

Employing the method of electric stimulation of deeply-placed points in the brain stem by means of a stereotaxic instrument, a method described in the first part of these "Beiträge," the author describes a series of experiments designed to reveal the nervous control of the circulation and of respiration by the brain stem, and to identify the structures—nuclei and paths—concerned in this regulation.

A long historical review precedes the descriptive experimental matter which comprises the bulk of the monograph.

*The Adrenal Cortex and Intersexuality.* By L. R. Broster, Clifford Allen, H. W. C. Vines, Jocelyn Patterson, Alan W. Greenwood, G. F. Marrian, and G. C. Butler. With a foreword by Sir Walter Langdon-Brown. Demy 8vo. Pp. 245, with numerous illustrations and charts. London: Chapman and Hall. Price 15s. net.

A book compounded by no less than seven authors, approaching a subject of profound interest and importance from clinical, psychological, pathological, and bio-chemical angles.

The outstanding feature of the publication is the correlation of virilism and sexual disturbances with histological variations within the adrenal cortex and the associated excretion within the urine of specific bio-chemical substances. The histological change is apparent in a fuchsinophil staining of cells of the adrenal cortex. It is a little strange, perhaps, that some of the cases which depict most histological evidence of virilism fail to exhibit free male hormone in the urine.

Numerous clinical cases are cited in illustrating the four groups into which the authors have arranged their cases. The groups consist of: prepubertal virilism, postpubertal virilism, Achard-Thiers Syndrome, and postmenopausal virilism. The cases in the first two of these groups are benefited by surgery, the other groups are best treated by glandular therapy. Particular attention is drawn to the importance of the early instigation of treatment owing to the protracted influences underlying such changes, and the permanence of the induced characteristics.

The diagnosis is somewhat difficult, so much so that laparotomy is advised to this end: perhaps somewhat lightly, as when recommended in children presenting

hypertrophic change in the clitoris. Laparotomy is essential to the exclusion of disorders of other glands, to ensure the presence of both suprarenals and determine which is the larger, to exclude the presence of accessory suprarenals, and in order to investigate the state of development of the internal genitalia. The post-operative period is apt to be stormy, hence the operation of adrenalectomy demands good physical resources on the part of the patient.

The results of operation are said to indicate a general and immediate tendency to lose acquired male characteristics with return to normal sexuality psychologically: these results, however, do not appear to be quite so obvious in some of the contained case reports. Hirsutism, although diminished, appears to persist in varying degrees, necessitating depilation by the patient. (Group I cases observed after a period of ten years are reported thus: "can control their hirsuties and though they have not menstruated or changed much progress of the disease appears to have been arrested.")

The pathological study is a valuable and commendable contribution to the knowledge of adrenal function in its mechanism of control of sexual development. Some of the suggestions are hypothetical. It is disappointing to note that in advocating the application of the pre-operative free hormone test such was not adhered to for "owing to the time taken to perform it it has not been utilised in this series." The section deals very clearly with the relationship of the suprarenal to Cushing's Disease and like conditions, and the relative parts played by chromosomal and endocrinal factors in the sexual pattern. The bi-sexual qualities of the secretions of the adrenal cortex explain the instability of the female sexuality relative to that of the male.

The illustrations are excellent but additions could be made with advantage showing the macroscopic and microscopic changes in the adrenals.

The book is thoroughly recommended to all interested in the endocrinology of sexual function and development.

*A Biological Approach to the Problem of Abnormal Behaviour.* By Milton Harrington, M.D. Lancaster (U.S.A.): Science Press Printing Company. 1938. Pp. 459.

Like other serious attempts to take the "fundamental facts of anatomy, physiology, medicine and general biology, together with the facts of normal and abnormal psychology, and to build a theory which will harmonize with this large and widely diversified group of facts," Dr. Harrington's book is more easily praised for the purity of its intentions than for the success with which they have been carried out. The cause of the author's failure lies not so much in himself as in the incompleteness of his material: the time for a full synthesis is not yet. Disapproving entirely of the psychoanalytical doctrine, which he criticizes effectively, he has aimed at a mechanistic view of the behaviour of man as a social organism. The outcome is a broad, theoretical survey, acceptable enough and even valuable until we go beyond the surface outlines of abnormal psychology to consider the details of conduct, especially in mental disorder. It also falls short in its grasp of the physiology of the nervous system, as now conceived, and of modern psychology. It is, however, clearly written, interesting, and well designed.

*Some Investigations into the Physiology of Emotions.* By H. I. Schou, M.D. London: Humphrey Milford. 1937. Pp. 111. Price 8s.

So painstaking an investigation as this into some bodily concomitants of mild emotion is particularly valuable now that psycho-somatic relationships are being widely assumed and discussed. With neurotic patients as his subjects, Dr. Schou studied blushing, skin temperature, basal metabolic rate, insensible perspiration, gastric secretion, blood sugar curve, and adrenalin content in the blood. Although the technical procedures are not always those best suited to the inquiry, the findings seem reliable and instructive as far as they go. Whether these observations on weak transient emotional changes in neurotic persons can be extended and applied to the more lasting affective anomalies is questionable. There is, moreover, in this report hardly enough emphasis on the still unaccountable wide individual differences in the physiological manifestations of emotion.

*Schizophrenie und Mord: Ein Beitrag zur Biopsychopathologie des Mordes.* By Dr. Nikola Schipkowensky. Berlin: Springer. 1938. Pp. 186. Price RM. 18.

The value of this monograph lies chiefly in the sixteen case-reports, withdrawn from the records of the Munich psychiatric clinic. They serve as the text for a discursive "contribution on the biopsychopathology of murder," much of which is polemical and designed to show how untenable are the views of Lombroso and of Freud. The writer's own conclusions are so vague, expressed as they partly are in terms of "fundamental dynamics of primitive psychic structures," "the specific human instinct of striving after happiness," "the fundamental experience of association between individual, genus, and cosmos," &c., as to be too obscure for examination. The clinical psychiatric comments and the observations on suicidal tendencies in these patients are informative, and the opening sections on biological and anthropological issues interesting but superficial. A rather irrelevant chapter deals with the problem of dreams in relation to psychosis and murder.

*Die Psychologie und Psychopathologie der Hysterie.* By Dr. Robert Flinker. Leipzig: Thieme. 1938. Pp. 63. Price RM. 4·20.

This is yet another attempt to explain hysteria, in which the author does not bring forward original observations but only his re-arrangement of current views (especially those of Kretschmer), and selects from books he has read evidence to support his belief that an anomaly of purposeful activity is at the root of hysteria. In spite of much detail, the treatment of the subject is superficial, and more suited to an essay than to a monograph.

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**SUNDAY,** August 20. 9 p.m. — Informal meeting at the Restaurant Nimb.

**MONDAY,** August 21. 9.30 a.m. — Official opening of the Congress at the Rigsdag Building.

10 a.m. DISCUSSION: **The Endocrine-Vegetative System with special reference to Neurology.**

*Chairman:* Professor L. VAN BOGAERT.

*Rapporteurs:* Professor Sir HENRY DALE (London). Intervention des médiateurs chimiques dans la transmission des excitations, comme neuro-effecteurs et connecteurs intraneuraux dans le systéme autonome et leur relation avec l'appareil endocrinien.

Dr. LARUELLE (Bruxelles). Les bases anatomiques du systéme autonome bulbo-spinal et cortical.

Professor FULTON (New Haven). Physiologie du systéme autonome cortical et bulbospinal dans sa connexion avec l'appareil endocrinien.

Dr. O. FOERSTER (Breslau). Die Beziehungen von Hypophyse und andere endokrinen Drüsen zum neuro-vegetativen System.

Dr. FORSBERG (Oslo). Die Beziehungen der endokrinen Drüsen zu den Muskelfunktionen unter besonderer Berücksichtigung der Myopathien.

2 p.m. CONTINUATION OF THE DISCUSSION.

*Chairman:* Professor H. PETTE.

8 p.m. RECEPTION at the Town Hall by invitation of the Corporation of Copenhagen.

**TUESDAY,** August 22.

9.30 a.m. Discussion : **The Heredo-familial Disease, especially from the Genetic Aspect.**

*Chairman :* Professor G. Guillain.

*Rapporteurs :* Professor B. Sachs (New York). L'idiotie familiale amaurotique et ses relations avec les autres maladies héréditaires et familiales.

Professor Andre Thomas (Paris). Les maladies héréditaires et familiales du system cerebelleux. L'heredo dégénération spino-cerebelleuse.

Professor Jonesco-Sisesti (Bucarest). Les affections extra-pyramidales. La dégénération hepatolenticulaire. La chorée de Huntington. Les myopathies. Les atrophies nucleaires. La neurofibromatose.

Professor Curtius (Berlin). Les maladies héréditaires du systéme nerveux au point de vue de la genetique.

Professor Schaffer (Budapest). L'anatomie pathologique generale des maladies héréditaires et familiales du systéme nerveux.

2 p.m. Continuation of the Discussion.

*Chairman :* Professor V. M. Buscaino.

**WEDNESDAY,** August 23. No scientific business. Excursions will be arranged for Frederiksborg Castle, Hillerød, Kronborg Castle, etc.

**THURSDAY,** August 24.

9.30 a.m. to 12.30 p.m. and 2 p.m. Short papers on various neurological and neurosurgical subjects.

8 p.m. Official Banquet.

**FRIDAY,** August 25.

9.30 a.m. Discussion : **Neurological Aspects of the Avitaminoses with special reference to the Peripheral Nervous System.**

*Chairman :* Professor G. H. Monrad-Krohn.

*Rapporteurs :* Professor Sir Edward Mellanby (London).
Professor G. C. Riquier (Pavia).
Dr. J. S. Wechsler (New York).
Dr. D. McAlpine (London).
Dr. H. P. Stubbe Teglbjaerg (Copenhagen).

2 p.m. Continuation of the Discussion.

Evening. Reception at H.M. the King's summer residence, Fredensborg Castle.

# REGULATIONS

## ACTIVE MEMBERSHIP

Applications for active membership from neurologists in Great Britain should be made to the **Secretary of the British National Committee**, Dr. MACDONALD CRITCHLEY, 137, Harley Street, London, W.1, to whom the subscription, **40 Danish Kroner**, should be paid.

## ASSOCIATE MEMBERSHIP

Is open to non-professional persons, men and women, interested in the Congress. The subscription is **20 Danish Kroner.**

## SCIENTIFIC CONTRIBUTIONS

Papers, either bearing on one of the three main subjects or on any aspect of neurological medicine or surgery, are invited. The maximum time allotted is ten minutes. Titles, together with an abstract not more than one hundred and fifty words long, should be sent to the Secretary of the British Committee, by April 1, 1939. If members wish to have their papers published in the Transactions of the Congress the typescript (not longer than 1,500 words) must be handed in at the Bureau before the end of the Congress. Authors must pay for their own illustrations **(10 to 17 Danish Kroner for the page).**

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